9/12/96

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 NEWS  1  Sep  6  STN Seminar Schedule - N. America
 NEWS  2  Sep 21  MAC & DOS STN Express Users
 NEWS  3  Aug  4  Macintosh STN Express Users of C(O)CH3 Shortcut
 NEWS  4  Jul 30  Use SDI EDIT to Change SDIs
 NEWS  5  Jul 30  Use SET ACCOUNT to Specify and Modify Online Cost
                  Centers
 NEWS  6  Jul 30  Use EDIT QUERY to Edit and Modify Online Queries
 NEWS  7  Jul 30  Use NOH Keyword to Suppress Highlighting
 NEWS  8  Aug 27  LINSPEC - Learning INSPEC File now Available
 NEWS  9  Aug 27  Engineering Index Thesaurus for COMPENDEX
 NEWS 10  Aug 27  AEROSPACE now Available
 NEWS 11  Aug 27  Use SET NOTICE to Monitor Display Charges
 NEWS 12  Sep  5  Derwent Manual Code Definitions now Echoed
 NEWS 13  Sep  9  Variable SDIs in API

 NEWS  HOURS  STN Operating Hours Plus Help Desk Availability
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Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 11:33:53 ON 16 SEP 96

=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    0.15        0.15

FILE 'REGISTRY' ENTERED AT 11:34:03 ON 16 SEP 96
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DICTIONARY FILE UPDATES: 13 SEPT 96  HIGHEST RN 180838-96-4

TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 1995

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> s lysine
L1       33725 LYSINE

=> s l1 and trasferrin
             0 TRASFERRIN
```

```
L2            0 L1 AND TRASFERRIN

=> s l1 and transferrin
           152 TRANSFERRIN
L3            0 L1 AND TRANSFERRIN

=> d l1 lc

L1   ANSWER 1 OF 33725  REGISTRY  COPYRIGHT 1996 ACS
LC   STN Files:   CAPLUS

=> fil caplus uspatfull biosis medline embase
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      11.11      11.26

FILE 'CAPLUS' ENTERED AT 11:35:09 ON 16 SEP 96
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=> s l1
TOO MANY TERMS FOR FILE CROSSOVER IN 'L1'
There are limits on the size of an answer set being crossed over from
one file to another.  Enter "HELP CROSSOVER" at an arrow prompt (=>)
for specific information.

=> s transferrin
L4        11155 FILE CAPLUS
L5         1252 FILE USPATFULL
L6        14932 FILE BIOSIS
L7        13901 FILE MEDLINE
L8        11310 FILE EMBASE

TOTAL FOR ALL FILES
L9        52550 TRANSFERRIN

=> s l9 and poly(w)lysine
L10           4 FILE CAPLUS
L11           4 FILE USPATFULL
L12           2 FILE BIOSIS
L13           2 FILE MEDLINE
L14           2 FILE EMBASE

TOTAL FOR ALL FILES
L15          14 L9 AND POLY(W) LYSINE

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           8 DUP REM L15 (6 DUPLICATES REMOVED)
```

=> d ibib ab 1-

L16 ANSWER 1 OF 8 USPATFULL
ACCESSION NUMBER: 96:46146 USPATFULL
TITLE: Conjugates for introducing nucleic acid into higher eucaryotic cells
INVENTOR(S): Curiel, David T., Chapel Hill, NC, United States
Hu, Ping-chuan, Chapel Hill, NC, United States
Birnstiel, Max L., Vienna, Austria
Cotten, Matthew, Vienna, Austria
Wagner, Ernst, Langenzersdorf, Austria
PATENT ASSIGNEE(S): Boehringer Ingelheim International, GmbH, South San Francisco, Germany, Federal Republic of (non-U.S. corporation)
Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
University of North Carolina at Chapel Hill, Chapel Hill, NC, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5521291	960528

APPLICATION INFO.: US 93-166899 931215 (8)
RELATED APPLN. INFO.: Continuation of Ser. No. US 92-949205, filed on 23 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-864758, filed on 7 Apr 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-827049, filed on 30 Jan 1992, now abandoned which is a continuation-in-part of Ser. No. US 91-767787, filed on 30 Sep 1991, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Feisee, Lila
LEGAL REPRESENTATIVE: Sterne, Kessler, Goldstein & Fox
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 23 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 2406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Conjugates in which a virus is bound via an antibody to a substance having an affinity for nucleic acid, for transporting gene constructs into higher eucaryotic cells. Complexes of the conjugates and nucleic acid are internalized in the cell, whilst the virus as part of the complex brings about the internalization and the release of the contents of the endosomes, in which the complexes are located after entering the cell. Pharmaceutical preparations in which the nucleic acid is a therapeutically active gene construct, particularly for use in gene therapy.

L16 ANSWER 2 OF 8 USPATFULL
ACCESSION NUMBER: 95:75727 USPATFULL
TITLE: Peptide-metal ion pharmaceutical preparation and method
INVENTOR(S): Zamora, Paul O., Albuquerque, NM, United States
Rhodes, Buck A., Albuquerque, NM, United States
PATENT ASSIGNEE(S): Rhomed Incorporated, Albuquerque, NM, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5443816	950822

APPLICATION INFO.: US 92-840077 920220 (7)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 90-565275, filed on 8 Aug 1990, now patented, Pat. No. US 5102990, issued on 7 Apr 1992
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Geist, Gary
ASSISTANT EXAMINER: Chapman, Lara E.
LEGAL REPRESENTATIVE: Peacock, Deborah A.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 1553
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Peptides containing a biological-function domain and a medically useful metal ion-binding domain are labeled with medically useful metal ions for use in diagnosis and treatment of a variety of pathologic conditions. The peptides have the amino acid sequence

(R.sub.1)-[Y.sub.1].sub.n -(R.sub.2),

(R.sub.1)-[Y.sub.1 -(R.sub.2)-Y.sub.1].sub.n -(R.sub.3)

and (R.sub.1)-[Y.sub.1 -(R.sub.2)-Y.sub.2].sub.n -(R.sub.3)

wherein the medically useful metal ion-binding domain is [Y.sub.1].sub.n, [Y.sub.1 -(R.sub.2)-Y.sub.1].sub.n or [Y.sub.1 -(R.sub.2)-Y.sub.2].sub.n in which n is a number between 1 and about 6 and Y.sub.1 and Y.sub.2 are amino acids with a sulfur, nitrogen or oxygen which is available for binding to metal ions, or can be made available for binding to metal ions; the biological-function domain is an amino acid sequence containing from 1 to about 20 amino acids located in any one or more of R.sub.1, R.sub.2 or R.sub.3 ; and those portions of R.sub.1, R.sub.2 and R.sub.3 which are not part of the biological-function domain are amino acid sequences containing from 0 to about 20 amino acids. The resulting product may be stored frozen or lyophilized, with labeling accomplished by the addition of the medically useful metal ions. The medically useful metal ion may be radioactive or paramagnetic, with diagnosis performed by gamma scintigraphy, specific photon emission computerized tomography, positron emission tomography or magnetic resonance imaging.

L16 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1996 ACS DUPLICATE 1
ACCESSION NUMBER: 1995:78661 CAPLUS
DOCUMENT NUMBER: 122:177804
TITLE: Carbohydrate receptor-mediated gene transfer to human T leukemic cells
AUTHOR(S): Thurnher, Martin; Wagner, Ernst; Clausen, Henrik; Mechtler, Karl; Rusconi, Sandro; Dinter, Andre; Birnstiel, Max L.; Berger, Eric G.; Cotten, Matt
CORPORATE SOURCE: Institute of Physiology, University of Zurich, Zurich, CH 8057, Switz.
SOURCE: Glycobiology (1994), 4(4), 429-35
CODEN: GLYCE3; ISSN: 0959-6658
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mucin-type carbohydrate Tn cryptantigen (GalNAc.alpha.1-O-Ser/Thr, where GalNAc is N-acetyl-D-galactosamine) is expressed in many carcinomas, in hemopoietic disorders including the Tn syndrome, and on human immunodeficiency virus (HIV) coat glycoproteins, but is not expressed on normal, differential cells because of the

expression of a Tn-processing galactosyltransferase. Using Jurkat T leukemic cells which express high levels of Tn antigen due to deficient Tn galactosylation, the authors have established the Tn antigen-mediated gene transfer and demonstrate the considerable efficiency of this approach. The authors used poly(L-lysine) conjugates of the monoclonal antibody 1E3 directed against the Tn antigen to deliver the luciferase and .beta.-galactosidase reporter genes to Jurkat cells by receptor-mediated endocytosis. Addn. of unconjugated 1E3 reduced transfection efficiency in a concn.-dependent manner and incubation with free GalNAc abolished DNA transfer completely, indicating that gene delivery is indeed mediated by the Tn antigen. Pre-treatment of Jurkat cells with Vibrio cholerae sialidase, which uncovers addnl. Tn antigens, resulted in an improvement of gene transfection. Both human and chicken adenovirus particles attached to the DNA/polylysine complex strongly augmented transgene expression. When the .beta.-galactosidase (lacZ) gene was delivered to Jurkat cells by Tn-mediated endocytosis, up to 60% of the cells were pos. in the cytochem. stain using 5-bromo-4-chloro-3-indolyl-.beta.-D-galactopyranoside (X-gal) as a chromogenic substrate. The efficiency of the **transferrin** receptor-mediated DNA uptake into Jurkat cells was comparatively low, although these cells were shown to express considerable amts. of **transferrin** receptor. The authors show here that a mucin-type carbohydrate antigen mediates highly efficient DNA uptake by endocytosis into Jurkat T cells. This method represents a 50-fold improvement of Jurkat cell transfection efficiency over other phys. gene transfer techniques. Specific gene delivery to primary cancer cells exhibiting Tn epitopes may esp. be desirable in immunotherapy protocols.

L16 ANSWER 4 OF 8 USPATFULL
ACCESSION NUMBER: 91:24753 USPATFULL
TITLE: Peptide inhibitors of motor neuron attachment to s-laminin
INVENTOR(S): Hunter, Dale D., St. Louis, MO, United States
Sanes, Joshua R., St. Louis, MO, United States
Merlie, John P., St. Louis, MO, United States
Adams, Steven P., St. Charles, MO, United States
PATENT ASSIGNEE(S): Washington University, St. Louis, MO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5003044	910326
APPLICATION INFO.:	US 89-382606	890719 (7)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Lee, Lester L.
ASSISTANT EXAMINER: Maebius, Stephen B.
LEGAL REPRESENTATIVE: Meyer, Scott J.; Williams, Jr., James W.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 519
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel peptides having inhibitor activity toward the binding of motor neurons to s-laminin are disclosed which are selected from the group consisting of

AEKQLREQVGDQYQTVRALAE

and fragments thereof containing the essential sequence LRE.

L16 ANSWER 5 OF 8 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1990:438167 CAPLUS
DOCUMENT NUMBER: 113:38167
TITLE: Human vascular smooth muscle cells in culture: growth characteristics and protein pattern by use of serum-free media supplements
AUTHOR(S): Dartsch, Peter C.; Weiss, Hans Dieter; Betz, Eberhard
CORPORATE SOURCE: Physiol. Inst. I, Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Eur. J. Cell Biol. (1990), 51(2), 285-94
CODEN: EJCBDN; ISSN: 0171-9335
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cultivation of vascular smooth muscle cells from human artery wall is possible under completely serum-free conditions. The effects of attachment factors on cell spreading and cell proliferation are described in detail as well as routine cultivation methods under serum-free conditions (clone cultures, cell migration, subcultivation by use of an exogenous trypsin inhibitor, cryopreservation, and readaptation of cells). After a careful adaptation period, only 2 (BMS and Ultroser G) of the 4 com. available serum-free media supplements tested were used successfully for a routine cultivation of the smooth muscle cells over several passages. With both supplements cell proliferation rates were comparable with hose obtained in medium contg. 10% fetal calf serum. The addn. of platelet-derived growth factor or **transferrin** to serum-free cultures had no growth-stimulating effect. The addn. of endothelial cell growth factor isolated from bovine brain caused a significant increase in proliferative activity in cells cultivated with BMS, but not with Ultroser G. Moreover, under the serum-free culture conditions described here, the .gamma.-actin content of the cells is largely reduced (51%) for cells cultivated in Ultroser G, and 12% for cells cultivated in BMS) when compared with cells cultivated under serum-contg. conditions (.gamma.-actin content = 100%). The .alpha.-actin content was obsd. to be unaltered. Even after a careful readaptation of serum-free cultured cells to serum conditions, the .gamma.-actin content remained reduced.

L16 ANSWER 6 OF 8 CAPLUS COPYRIGHT 1996 ACS DUPLICATE 2
ACCESSION NUMBER: 1990:484701 CAPLUS
DOCUMENT NUMBER: 113:84701
TITLE: Acid-sensitive dissociation between **poly (lysine)** and histamine-modified poly(glutamate) as a model for drug-releasing from carriers in endosomes
AUTHOR(S): Shen, Wei Chiang
CORPORATE SOURCE: Sch. Pharm., Univ. South. California, Los Angeles, CA, 90033, USA
SOURCE: Biochim. Biophys. Acta (1990), 1034(1), 122-4
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histamine was coupled to poly(L-glutamate) (PLG) to give a copolymer, poly(glutamylhistamineglutamate) (PHG), with approx. 40% of carboxyl groups in PLG being modified. Unlike either poly(L-histidine) (PLH) or PLG, PHG pptd. only in buffers with pH between 4 and 5. A complex was formed between PHG and poly(L-lysine) (PLL) at pH 7, but it was rapidly dissocd. at

.ltoreq. pH 5. When PHG-linked **transferrin** (Tf-PHG) was used to deliver a PLL-conjugated [3H]methotrexate ([3H]MTX-PLL) in K562 leukemia cell cultures, an intracellular accumulation of the radioactivity was obsd. These results suggest that a copolymer with both imidazole and carboxyl groups can be useful in the design of acid-sensitive, carrier-mediated drug delivery systems.

L16 ANSWER 7 OF 8 USPATFULL
ACCESSION NUMBER: 89:43422 USPATFULL
TITLE: Conjugation of aromatic amines or nitro-containing compounds with proteins or polypeptides by photoirradiation of the azide derivatives with ultraviolet light in order to produce antibodies against the haptens
INVENTOR(S): Hollenberg, Paul F., Skokie, IL, United States
Pandey, Ramendra N., Lombard, IL, United States
PATENT ASSIGNEE(S): Northwestsern University, Evanston, IL, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4835258	890530
APPLICATION INFO.:	US 86-946436	861224 (6)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Phillips, Delbert R.
ASSISTANT EXAMINER: Draper, Garnette D.
LEGAL REPRESENTATIVE: Tilton, Fallon, Lungmus and Chestnut
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 393
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of linking primary aromatic amine- or nitro-compounds to carrier proteins by photochemical reactions in order to produce antibodies against the haptens.

L16 ANSWER 8 OF 8 CAPLUS COPYRIGHT 1996 ACS DUPLICATE 3
ACCESSION NUMBER: 1987:48256 CAPLUS
DOCUMENT NUMBER: 106:48256
TITLE: Photochemical linking of primary aromatic amines to carrier proteins to elicit antibody response against the amine haptens
AUTHOR(S): Pandey, Ramendra N.; Davis, Lyman E.; Anderson, Byron; Hollenberg, Paul F.
CORPORATE SOURCE: Med. Sch., Northwest. Univ., Chicago, IL, 60611, USA
SOURCE: J. Immunol. Methods (1986), 94(1-2), 237-46
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A photolabeling approach for conjugating primary arom. amines to carrier proteins is reported which avoids some of the problems of other conjugation methods and which was used to elicit antibodies against the primary arom. amine hapten. The method described here is of general application for coupling primary arom. amines to the carrier proteins and circumvents many of the problems inherent in the isocyanate or diazocoupling methods. 3-Azido-N-ethylcarbazole (ANEC), the azido analog of 3-amino-N-ethylcarbazole, was conjugated to bovine serum albumin (BSA), human **transferrin** (TR), thyroglobulin (TH), **poly-(lysine** .cntdot.tyrosine), and **poly-(lysine** .cntdot.phenylalanine) using std. photolabeling procedures. After

photolysis, the conjugated proteins or polypeptides were sepd. from the unbound products of ANEC photolysis on a Sephadex G-10 column. The conjugated proteins were extd. with isobutanol which demonstrated that approx. 20% of the ANEC was covalently coupled to the protein carriers and that the larger portion of the arom. haptens was non-covalently and hydrophobically bound to the carriers. The ANEC-protein conjugates used for immunization demonstrated a total covalently and non-covalently bound ANEC epitope d. of 90 per BSA, 107 per TR, and 800 per TH mol. Rabbits were immunized with the 3 conjugated proteins and the prodn. of antibody specific for the 3-amino-N-ethylcarbazole hapten was demonstrated by ELISA and by inhibition studies using hapten-carrier conjugates of free hapten. The results demonstrate that antibodies against arom. amine haptens may be raised by immunizing animals with hapten-carrier protein conjugates produced by photolabeling. Since the coupling conditions are very mild and the functional group requirements are so general, most carrier proteins should be suitable for use in this method. Moreover, the method described is rapid and generates only small amts. of waste when compared to the diazocoupling and isocyanate coupling procedures. This coupling methodol. should be useful for producing antibodies against a variety of primary arom. amine carcinogens.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.87	29.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.85	-1.85

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 NEWS  4  Jul 30  Use SDI EDIT to Change SDIs
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                  Centers
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 NEWS 10  Aug 27  AEROSPACE now Available
 NEWS 11  Aug 27  Use SET NOTICE to Monitor Display Charges
 NEWS 12  Sep  5  Derwent Manual Code Definitions now Echoed
 NEWS 13  Sep  9  Variable SDIs in API

 NEWS  HOURS  STN Operating Hours Plus Help Desk Availability
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 NEWS  PHONE  Direct Dial and Telecommunication Network Access to STN
 NEWS  WWW    CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 08:53:28 ON 16 SEP 96

=> fil caplus biosis medline embase uspatful
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

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=> s cell? or tissue?
L1     1776074 FILE CAPLUS
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SEARCH ENDED BY USER
The search profile you entered was too complex or gave
too many answers. Simplify or subdivide the query and
try again. If you have exceeded the limit of 2 million
answers, enter "DELETE HISTORY" at an arrow prompt to remove
all previous answer sets and begin at L1. Use the SAVE
command to store any important profiles or answer sets before
using DELETE HISTORY.

=> s nucleic acid?
L2 64538 FILE CAPLUS
L3 25340 FILE BIOSIS
L4 113878 FILE MEDLINE
L5 17851 FILE EMBASE
L6 10302 FILE USPATFULL

TOTAL FOR ALL FILES
L7 231909 NUCLEIC ACID?

=> s l7 and (contrast or imag)
L8 1732 FILE CAPLUS
L9 694 FILE BIOSIS
L10 5794 FILE MEDLINE
L11 951 FILE EMBASE
L12 3566 FILE USPATFULL

TOTAL FOR ALL FILES
L13 12737 L7 AND (CONTRAST OR IMAG)

=> s l7 and (contrast or imag?)
L14 2115 FILE CAPLUS
L15 844 FILE BIOSIS
L16 6356 FILE MEDLINE
L17 1076 FILE EMBASE
L18 4095 FILE USPATFULL

TOTAL FOR ALL FILES
L19 14486 L7 AND (CONTRAST OR IMAG?)

=> s l19 and agent?
L20 161 FILE CAPLUS
L21 70 FILE BIOSIS
L22 272 FILE MEDLINE
L23 112 FILE EMBASE
L24 3039 FILE USPATFULL

TOTAL FOR ALL FILES
L25 3654 L19 AND AGENT?

=> s l25 and (dna or rna or deoxy ribo? or ribonucleic?)
L26 111 FILE CAPLUS
L27 53 FILE BIOSIS
L28 242 FILE MEDLINE
L29 94 FILE EMBASE
L30 2437 FILE USPATFULL

TOTAL FOR ALL FILES
L31 2937 L25 AND (DNA OR RNA OR DEOXY RIBO? OR RIBONUCLEIC?)

```
=> s l31 and chelat?
L32          10 FILE CAPLUS
L33           5 FILE BIOSIS
L34           5 FILE MEDLINE
L35           3 FILE EMBASE
L36         425 FILE USPATFULL

TOTAL FOR ALL FILES
L37         448 L31 AND CHELAT?

=> s l37 and (cancer or tumour? or tumor? or neoplas?)
L38           1 FILE CAPLUS
L39           0 FILE BIOSIS
L40           1 FILE MEDLINE
L41           2 FILE EMBASE
L42         254 FILE USPATFULL

TOTAL FOR ALL FILES
L43         258 L37 AND (CANCER OR TUMOUR? OR TUMOR? OR NEOPLAS?)

=> s l32 or l33 or l34 or l35
L44          10 FILE CAPLUS

SEARCH ENDED BY USER
SEARCH ENDED BY USER

=> d l32 ibib ab 1-

L32  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 1996 ACS
ACCESSION NUMBER:         1996:126626  CAPLUS
DOCUMENT NUMBER:          124:170022
TITLE:                    Immobilization of biologically active materials
                          and diagnostic agents in cross-linked
                          poly(organophosphazenes)
INVENTOR(S):              Allcock, Harry R.; Pucher, Shawn R.; Visscher,
                          Karyn B.
PATENT ASSIGNEE(S):       Penn State Research Foundation, USA
SOURCE:                   PCT Int. Appl., 59 pp.
                          CODEN: PIXXD2

                          NUMBER                    DATE
                          --------------            ------
PATENT INFORMATION:       WO 9532736 A1             951207
DESIGNATED STATES:        W:  AU, CA, JP, KR, NO
                          RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
                          LU, MC, NL, PT, SE
APPLICATION INFORMATION:  WO 95-US6854              950531
PRIORITY APPLN. INFO.:    US 94-251510              940531
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
AB   A polymeric material is disclosed that comprises a
     poly(organophosphazene) that contains at least (1) a substituent
     group that can be radiation crosslinked and (2) a substituent group
     that is susceptible to hydrolysis under the conditions of use, to
     impart biodegradability to the polymer, in combination with a
     substance to be delivered, e.g., drug, diagnostic imaging
   agent, biomol., enzyme, etc.

L32  ANSWER 2 OF 10  CAPLUS  COPYRIGHT 1996 ACS
ACCESSION NUMBER:         1991:224862  CAPLUS
```

DOCUMENT NUMBER: 114:224862
TITLE: Ultrastructural localization of **nucleic acids** in plant tissues following the use of malachite green or neutral red in the fixative solution
AUTHOR(S): Lawton, June R.
CORPORATE SOURCE: Electron. Microsc. Unit, Univ. Durban-Westville, Durban, 4000, S. Afr.
SOURCE: J. Microsc. (Oxford) (1990), 158(3), 343-54
CODEN: JMICAR; ISSN: 0022-2720
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Malachite green and neutral red, when added to glutaraldehyde for fixation of various tissues, yielded high-**contrast images** of cell ultrastructure. Malachite green, in acid conditions, appeared to increase **contrast** of heterochromatin material in the nucleus whereas neutral red gave greater clarity to the nucleolus and to cytoplasmic ribosomes. Control tissue fixed under acid conditions showed little damage but there were cryst. areas at the periphery of the nucleolus. RNase did not digest cytoplasmic ribosomes from tissue after neutral red-glutaraldehyde fixation. These results suggested that neutral red became bound to **RNA** in the tissues. Fixation with malachite green, at a pH below 6, did not affect the digestion of **RNA** by RNase but did protect chromatin against the bleaching action of the **chelating agent** EDTA. The addn. of malachite green (pH <6) or neutral red to glutaraldehyde are useful techniques for the investigation of the ultrastructure of nuclear material and cytoplasmic ribosomes.

L32 ANSWER 3 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1991:214455 CAPLUS
DOCUMENT NUMBER: 114:214455
TITLE: Pharmaceutical liposome and lipid complex compositions
INVENTOR(S): Szoka, Francis C., Jr.
PATENT ASSIGNEE(S): University of California, Oakland, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9011780 A1	901018
DESIGNATED STATES:	W: AU, CA, HU, JP, NO RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE	
APPLICATION INFORMATION:	WO 90-US1646	900328
PRIORITY APPLN. INFO.:	US 89-332609	890331
	US 89-334055	890405

DOCUMENT TYPE: Patent
LANGUAGE: English

AB Liposome and lipidic particle formulations of compds. are prepd. by dissolving the compds. in a soln. of liposome-forming lipids in an aprotic solvent such as DMSO, optionally contg. a lipid-solubilizing amt. of a lower alkanol, and injecting the resulting soln. into an aq. soln. The resulting liposome or lipidic particle suspension may be dialyzed or otherwise concd. This method is particularly useful for compds. which are poorly-sol. in aq. soln., but is generally useful for any compd.(s) which can be dissolved in an aprotic solvent or aprotic solvent/lower alkanol mixt. A soln. of doxorubicin (6.2 mM) in an EtOH soln. of egg phosphatidylglycerol-

egg phosphatidylcholine-cholesterol (7:3:6), at a 96.4 mM total lipid concn., was injected in 10 mM tris-HCl (pH 4) contg. 140 mM NaCl. The lipid suspension was dialyzed against the above aq. phase and the encapsulated doxorubicin was sepd. by column chromatog. on Sephadex G-50.

L32 ANSWER 4 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1990:472468 CAPLUS
DOCUMENT NUMBER: 113:72468
TITLE: Transferrin-polycation-mediated introduction of **DNA** into human leukemic cells: stimulation by **agents** that affect the survival of transfected **DNA** or modulate transferrin receptor levels
AUTHOR(S): Cotten, Matt; Laengle-Rouault, Francoise; Kirlappos, Helen; Wagner, Ernst; Mechtler, Karl; Zenke, Martin; Beug, Hartmut; Birnstiel, Max L.
CORPORATE SOURCE: Res. Inst. Mol. Pathol., Vienna, A-1030, Austria
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(11), 4033-7
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors subverted a receptor-mediated endocytosis event to transport genes into human leukemic cells. By coupling the natural iron-delivery protein transferrin to the **DNA**-binding polycations polylysine or protamine, protein conjugates were created that bind **nucleic acids** and carry them into the cell during the normal transferrin cycle (Wagner, E. et al., 1990). This procedure is useful for a human leukemic cell line. The rate of gene delivery was enhanced by (1) increasing the transferrin receptor d. through treatment of the cells with the cell-permeable iron **chelator** desferrioxamine, (2) interfering with the synthesis of heme with succinyl acetone treatment, or (3) stimulating the degrdn. of heme with cobalt chloride treatment. Consistent with gene delivery as an endocytosis event, the subsequent expression in K-562 cells of a gene included in the transported **DNA** depends upon the cellular presence of the lysosomotropic **agent** chloroquine. By **contrast**, monensin blocks "transferrinfection," as does incubation of the cells at 18.degree..

L32 ANSWER 5 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1989:489889 CAPLUS
DOCUMENT NUMBER: 111:89889
TITLE: Novel diastereomers with opposite chirality at ruthenium formed by N7,.alpha.-PO4 **chelation** of 5'-dGMP to the antimetastatic **agent** trans-RuCl2(DMSO)4: NMR and CD evidence
AUTHOR(S): Alessio, Enzo; Xu, Yinghai; Cauci, Sabina; Mestroni, Giovanni; Quadrifoglio, Franco; Viglino, P.; Marzilli, Luigi G.
CORPORATE SOURCE: Dep. Chem. Sci., Univ. Trieste, Trieste, 34127, Italy
SOURCE: J. Am. Chem. Soc. (1989), 111(18), 7068-71
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CJACS
AB A novel diastereomeric pair of isomers was discovered in an initial

study of the interaction of the antimetastatic **agent** trans-RuCl2(DMSO)4, with **nucleic acid** components. In particular, 5'-dGMP forms 2 products that have characteristic features clearly indicating that the guanine N7 and the .alpha.-phosphate group form a **chelate** to the metal center. These features include (a) a pronounced downfield shift of the 31P NMR signals of the **chelates**; (b) a downfield shift of the H8 1H NMR signals of the guanine in the **chelates** -this downfield shift persists in monodentate N7 coordinate forms favored by protonation of the phosphate group at acid pH; and (c) characteristic changes in the shifts and coupling consts. of the deoxyribose 1H NMR signals. This unusual **chelation** mode of binding was characterized by NMR spectroscopy in only 2 previous studies. Interestingly, these studies involved other classes of metalloanticancer **agents**, namely Pt(II) and metallocene drugs. However, in these latter classes of drugs, only 1 isomer was possible. In the Ru derivs. studied here, the octahedral configuration led to the possibility of diastereomers. After sepn. of the **chelates** by HPLC, the isomers had nearly identical UV absorption spectra and a weak visible band at .apprx.410 nm. However, the CD spectra had bands with opposite signs but similar intensities and positions. Thus, the compds. are isomers that differ principally by having an opposite chirality at Ru. Anal. of several types of expts. demonstrated that the isomers have the compn., [Ru(II)Cl(H2O)(DMSO)2(5'-dGMP)]-. In **contrast** to the widely studied Pt(II) anticancer **agents**, the Ru drug does not readily bind to two 5'-dGMP at neutral pH. Thus, in addn. to stereochem. differences between the octahedral Ru(II) and square-planar Pt(II) drugs, the Ru(II) compds. may not easily form the N7,N7 GpG crosslink characteristic of the **DNA** adducts formed by Pt anticancer drugs. Should the Ru(II) drugs form such a crosslink form, however, 2 diastereomers, with opposite chirality at Ru, are possible.

L32 ANSWER 6 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1986:202885 CAPLUS
DOCUMENT NUMBER: 104:202885
TITLE: Inhibition of Euglena gracilis and wheat germ zinc **RNA** polymerases II by 1,10-phenanthroline acting as a **chelating agent**
AUTHOR(S): Mazus, B.; Falchuk, K. H.; Vallee, Bert L.
CORPORATE SOURCE: Cent. Biochem. Biophys. Sci. Med., Brigham and Women's Hosp., Boston, MA, 02115, USA
SOURCE: Biochemistry (1986), 25(10), 2941-5
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CJACS

AB Cu complexes of 1,10-phenanthroline (OP-Cu) hydrolyze **DNA**. This reaction was studied to det. whether 1,10-phenanthroline (OP) inhibition of the **RNA** and **DNA** polymerases result from template hydrolysis or the **chelation** of a metal assocd. with and essential to the function of these enzymes. Addn. of 4',6-diamino-2-phenylindole-di-HCl (DAPI) to **DNA** generated a fluorescence signal with a linear increase of the intensity over a broad range of **DNA** concns. from 0 to 100 .mu.g/mL. The progress of hydrolysis of **DNA** by DNase I or OP (2 mM) was monitored by the time-dependent decrease in DAPI-induced fluorescence. In the presence of OP, the rate of hydrolysis increased as the Cu2+ concn. in the reaction mixt. rose

from 10-8 to 10-5M. The rate differed for each **nucleic acid** template used; susceptibility to hydrolysis increased in the order poly(dA-dT) > denatured **DNA** > double-stranded **DNA**. However, millimolar amts. of OP did not hydrolyze the template even in the presence of Cu2+ (10-6M) when **DNA** was complexed with either Escherichia coli **DNA** polymerase I or E. gracilis or wheat germ **RNA** polymerase II. Under the same conditions, OP inhibited the activity of both varieties of **RNA** polymerase II with pKi values of 3.4 and 3.0, resp. The addn. of neocuproine from 10-5 to 10-3 M to **chelate** any Cu2+ present in the reaction mixt. did not change this inhibition. In **contrast**, OP did not affect **DNA** polymerase I. Thus, OP inhibits the enzyme activity of a complex of **RNA** polymerase with **nucleic acid** template by **chelation** of metal atoms essential for the function of these polymerases rather than by hydrolysis of their template. Zn was the only enzymically active metal assocd. with **RNA** polymerases. This functional role was confirmed further by the demonstration that these enzymes were also inhibited by other **chelating agents** whose structures differed distinctively from that of OP, including dipicolinic acid, 8-hydroxyquinoline, .alpha.,.alpha.'-bipyridyl, and 8-hydroxyquinoline-5-sulfonic acid.

L32 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1985:435479 CAPLUS
DOCUMENT NUMBER: 103:35479
TITLE: Modulation of transferrin receptor expression by inhibitors of **nucleic acid** synthesis
AUTHOR(S): Hedley, David; Rugg, Catherine; Musgrove, Elizabeth; Taylor, Ian
CORPORATE SOURCE: Ludwig Inst. Cancer Res., Univ. Sydney, Sydney, 2006, Australia
SOURCE: J. Cell. Physiol. (1985), 124(1), 61-6
CODEN: JCLLAX; ISSN: 0021-9541
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of the Fe **chelator** desferrioxamine (DFOA) on the expression of transferrin receptors (TfR) by CCRF-CEM human T-cell leukemia and B16 mouse melanoma cells growing in tissue culture were studied. DFOA enhanced TfR expression when added in the dose range of 10-5-10-4M to CCRF-CEM cells, but was toxic to these cells, with the lower concns. producing a slowing of cell growth with a buildup in S-phase, whereas higher concns. caused cell death with a block at the G1/S-phase interface. These toxic effects are compatible with its previously reported inhibition of the nonheme-Fe-contg. (M2) subunit of ribonucleotide reductase. In marked **contrast**, DFOA caused the growth of B16 melanoma cells to arrest in G1, without loss of cloning efficiency, and resulted in a fall in TfR expression to .apprx.50% of control values. Thus, the effects of DFOA on TfR expression may be linked to **DNA** synthesis rather than to a more generalized inhibition of Fe-dependent cellular processes. Inhibition of the M2 subunit of ribonucleotide reductase in CCRF-CEM cells with 5 .times. 10-5M hydroxyurea, which is not an Fe **chelator**, also enhanced TfR expression, as did thymidine and cytosine arabinoside, which have different enzyme targets. By measuring cellular **DNA** and **RNA** content simultaneously, it was shown that all of these **agents** caused unbalanced growth, i.e., inhibited **DNA** synthesis more than **RNA** synthesis.

In **contrast**, 6-thioguanine was more inhibitory to **RNA** synthesis, and treatment with this drug caused a fall in TfR expression. Thus, although CCRF-CEM cells treated with DFOA show enhanced TfR expression, similar effects are also seen with other inhibitors of **DNA** synthesis, provided that **RNA** synthesis is allowed to continue. These results provide further evidence that the regulation of TfR expression by proliferating cells is specifically linked to **DNA** synthesis rather than to the Fe requirements of other cellular processes.

L32 ANSWER 8 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1976:573448 CAPLUS
DOCUMENT NUMBER: 85:173448
TITLE: Euglena gracilis **DNA** dependent **RNA** polymerase II: a zinc metalloenzyme
AUTHOR(S): Falchuk, Kenneth H.; Mazus, Barbara; Ulpino, Lesbia; Vallee, Bert L.
CORPORATE SOURCE: Dep. Biol. Chem., Harvard Med. Sch., Boston, Mass., USA
SOURCE: Biochemistry (1976), 15(20), 4468-75
CODEN: BICHAW
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Zn is essential for cellular proliferation. Zn deficiency of E. gracilis results in arrest of cell division and deranges **nucleic acid** and protein metab., pointing to a decisive role of Zn in transcription and translation. Therefore, the role of Zn was investigated in the function of the **DNA** -dependent **RNA** polymerases (I) of this organism. Two I from Zn-sufficient organisms were purified by affinity chromatog. on a **DNA**-cellulose column and subsequently sepd. on DEAE-Sephadex A-25. The 2 fractions were characterized as I I and II by their elution pattern from DEAE-Sephadex and sensitivity to .alpha.-amanitin. I II has a provisional mol. wt. of 700,000 and contains an av. of 2.2 g-atoms of Zn/mole of enzyme, but no Mn, Cu, or Fe, as measured by microwave emission spectroscopy. **Chelating agents**, such as 1,10-phenanthroline (II), 8-hydroxyquinoline, 8-hydroxyquinoline-5-sulfonic acid, and lomofungin, inhibit activity. In **contrast**, the nonchelating analogs, 1,7- and 4,7-phenanthroline, do not affect activity. Inhibition by II is instantaneous and fully reversible by diln. II also inhibits I I, suggesting a role of Zn in its function. The demonstration that I II is a Zn enzyme indicates the involvement of Zn in eukaryotic **RNA** synthesis and serves as a further basis for the definition of the role of this element in eukaryotic cell growth, division, and differentiation.

L32 ANSWER 9 OF 10 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1970:528586 CAPLUS
DOCUMENT NUMBER: 73:128586
TITLE: Release of radioactive **nucleic acids** and mucoproteins by trypsin and ethylenediaminetetra-acetate treatment of baby-hamster cells in tissue culture
AUTHOR(S): Snow, Christine; Allen, Adrian
CORPORATE SOURCE: Dep. Biochem., Univ. Newcastle upon Tyne, Newcastle upon Tyne, Engl.
SOURCE: Biochem. J. (1970), 119(4), 707-14
CODEN: BIJOAK
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Monolayers of baby-hamster kidney cells were grown on glass in tissue culture and harvested with trypsin or EDTA in order to investigate the cell surface macromols. removed by these cell-disaggregating **agents**. The release of **nucleic acids** from the cells during the harvesting procedure was monitored by labeling the cellular **RNA** with uridine-5-3H and the cellular **DNA** with thymidine-2-14C. Treatment of the cells with EDTA caused an increase in the permeability of the plasma membrane with 7.6% of the cellular **RNA**, but less than 1% of the cellular **DNA**, being released. Moreover, 61% of the cells harvested with EDTA were permeable to trypan blue. With crude trypsin, lysis of the cell occurred with the release of similar amts. of **RNA** and **DNA** amounting to about 11% of the total cellular **nucleic acid**. In **contrast** cryst. trypsin released only 1% of the cellular **nucleic acids**. Since virtually all the cells (99%) after harvesting in cryst. trypsin were impermeable to trypan blue, this method was suitable for obtaining cell surface macromols. without contamination by intracellular damage. Glucosamine-1-14C was incorporated by the cells only into bound hexosamines and sialic acids. By monitoring the release of radioactivity in high-mol.-wt. material in such expts. a measure of the release of macromols. contg. amino sugars was obtained. Of the total macromols. contg. amino sugars in the cells 33%, 24% and 13% were released when the cells were harvested with crude trypsin, cryst. trypsin or EDTA, resp. Cryst. trypsin also released 39% of the total sialic acid of the cell, whereas less than 1% of the cellular sialic acid was present in the EDTA-treated fraction. The macromols. contg. amino sugars released with crude trypsin and EDTA are likely to be heavily contaminated with intracellular material. However, the macromols. released by cryst. trypsin appear to come from the cell surface.

L32 ANSWER 10 OF 10 CAPLUS COPYRIGHT 1996 ACS

ACCESSION NUMBER: 1967:410050 CAPLUS

DOCUMENT NUMBER: 67:10050

TITLE: Metabolic effects of copper in intact cells; comparative activity of cupric chloride and the cupric **chelate** of kethoxal bis(thiosemicarbazone)

AUTHOR(S): Booth, Barbara A.; Sartorelli, Alan C.

CORPORATE SOURCE: Sch. of Med., Yale Univ., New Haven, Conn., USA

SOURCE: Mol. Pharmacol. (1967), 3(3), 290-302
CODEN: MOPMA3

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The exposure of sarcoma 180 ascites cells to the cupric **chelate** [Cu(II)KTS] of kethoxal bis(thiosemicarbazone) (KTS) resulted in the death of a large proportion of the cell population; both the ligand portion of the mol., KTS, and CuCl2 were less toxic. Cells isolated from mice treated with Cu(II)KTS contained considerably greater amts. of Cu than did those cells exposed to the same no. of gram-atoms of Cu presented as either CuCl2 or Cu stearate. The relatively lipid-sol. **chelate**-form of Cu was evidently more readily assimilated. Dissocn. of Cu(II)KTS occurred within neoplastic cells, and this resulted in a relatively rapid loss from the cells of the ligand portion, KTS. In **contrast**, the Cu derived from Cu(II)KTS persisted for a much longer period of time. The relation of **nucleic acid** and protein synthesis to the phenomenon of cell death

induced by these **agents** was assessed by measuring the effects of the compds. on these metabolic processes. The formation of **DNA** was more sensitive to the inhibitory action of Cu(II)KTS, CuCl2, and KTS, than were either the syntheses of **RNA** or protein. In agreement with the cellular toxicity, Cu(II)KTS caused more pronounced depression of the incorporation of isotopic precursors into **DNA** than did either CuCl2 or KTS. The Cu present in cells treated with Cu(II)KTS induced at least 3 metabolic blocks on the pathways of **DNA** biosynthesis. The most sensitive site was measured by the incorporation of thymidine-3H into **DNA** and presumably was the result of the loss of activity of thymidine kinase. The findings obtained using a variety of isotopic precursors of **DNA** as biochem. probes suggested that the intracellular localization of Cu derived from Cu(II)KTS differed from that of CuCl2. 28 references.

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L33 ANSWER 1 OF 5 BIOSIS COPYRIGHT 1996 BIOSIS
ACCESSION NUMBER: 90:426106 BIOSIS
DOCUMENT NUMBER: BA90:86907
TITLE: ULTRASTRUCTURAL LOCALIZATION OF **NUCLEIC ACIDS** IN PLANT TISSUES FOLLOWING THE USE OF MALACHITE GREEN OR NEUTRAL RED IN THE FIXATIVE SOLUTION.
AUTHOR(S): LAWTON J R
CORPORATE SOURCE: ELECTRON MICROSCOPE UNIT, UNIV. DURBAN-WESTVILLE, P BAG X54001, DURBAN 4000, SOUTH AFRICA.
SOURCE: J MICROSC (OXF) 158 (3). 1990. 343-354. CODEN: JMICAR ISSN: 0022-2720
LANGUAGE: English
AB Malachite green and neutral red, when added to glutaraldehyde for fixation of various tissues, yielded high-**contrast** **images** of cell ultrastructure. Malachite green, in acid conditions, appeared to increase **contrast** of heterochromatin material in the nucleus whereas neutral red gave greater clarity to the nucleolus and to cytoplasmic ribosomes. Control tissue fixed under acid conditions showed little damage but there were 'crystalline' areas at the periphery of the nucleolus. RNase did not digest cytoplasmic ribosomes from tissue after neutral red glutaraldehyde fixation. These results suggested that neutral red became bound to **RNA** in the tissues. Fixation with malachite green, at a pH below 6, did not affect the digestion of **RNA** by RNase but did protect chromatin against the bleaching action of the **chelating agent** EDTA. The addition of malachite green (pH < 6) or nuetral red to glutaraldehyde are useful techniques for the investigation of the ultrastructure of nuclear material and cytoplasmic ribosomes.

L33 ANSWER 2 OF 5 BIOSIS COPYRIGHT 1996 BIOSIS
ACCESSION NUMBER: 90:354090 BIOSIS
DOCUMENT NUMBER: BA90:50669
TITLE: TRANSFERRIN-POLYCATION-MEDIATED INTRODUCTION OF **DNA** INTO HUMAN LEUKEMIC CELLS STIMULATION BY **AGENTS** THAT AFFECT THE SURVIVAL OF TRANSFECTED **DNA** OR MODULATE TRANSFERRIN RECEPTOR LEVELS.
AUTHOR(S): COTTEN M; LANGLE-ROUAULT F; KIRLAPPOS H; WAGNER E; MECHTLER K; ZENKE M; BEUG H; BIRNSTIEL M L
CORPORATE SOURCE: RES. INST. MOL. PATHOL., DR. BOHR-GASSE 7, A-1030 VIENNA, AUSTRIA.

SOURCE: PROC NATL ACAD SCI U S A 87 (11). 1990. 4033-4037. CODEN: PNASA6 ISSN: 0027-8424

LANGUAGE: English

AB We have subverted a receptor-mediated endocytosis event to transport genes into human leukemic cells. By coupling the natural iron-delivery protein transferrin to the **DNA**-binding polycations polylysine or protamine, we have created protein conjugates that bind **nucleic acids** and carry them into the cell during the normal transferrin cycle [Wagner, E., Zenke, M., Cotten, M., Beug, H & Birnstiel, M.L. (1990) Proc. Natl. Acad. Sci. USA 87, 3410-3414]. We demonstrate here that this procedure is useful for a human leukemic cell line. We enhanced the rate of gene delivery by (i) increasing the transferrin receptor density through treatment of the cells with the cell-permeable iron **chelator** desferrioxamine, (ii) interfering with the synthesis of heme with succinyl acetone treatment, or (iii) stimulating the degradation of heme with cobalt chloride treatment. Consistent with gene delivery as an endocytosis event, we show that the subsequent expression in K-562 cells of a gene included in the transported **DNA** depends upon the cellular presence of the lysosomotropic **agent** chloroquine. By **contrast**, monensin blocks "transferrinfection", as does incubation of the cells at 18.degree. C.

L33 ANSWER 3 OF 5 BIOSIS COPYRIGHT 1996 BIOSIS

ACCESSION NUMBER: 89:495369 BIOSIS

DOCUMENT NUMBER: BA88:121906

TITLE: NOVEL DIASTEREOMERS WITH OPPOSITE CHIRALITY AT RUTHENIUM FORMED BY N7 ALPHA PHOSPHATE **CHELATION** OF 5' DEOXY-GMP TO THE ANTIMETASTATIC **AGENT** TRANS RUTHENIUM DICHLORIDE DMSO-4 NMR AND CD EVIDENCE.

AUTHOR(S): ALESSIO E; XU Y; CAUCI S; MESTRONI G; QUADRIFOGLIO F; VIGLINO P; MARZILLI L G

CORPORATE SOURCE: DEP. CHEM. SCI., UNIV. TRIESTE, 34127 TRIESTE, ITALY.

SOURCE: J AM CHEM SOC 111 (18). 1989. 7068-7071. CODEN: JACSAT ISSN: 0002-7863

LANGUAGE: English

AB A novel diastereomeric pair of isomers was discovered in an initial study of the interaction of the antimetastatic **agent** trans-RuCl2(DMSO)4 with **nucleic acid** components. In particular, 5'-dGMP forms two products that have characteristic features clearly indicating that the guanine N7 and the .alpha.-phosphate group form a **chelate** to the metal center. These features include (a) a pronounced downfield shift of the 31P NMR signals of the **chelates**; (b) a downfield shift of the H8 1H NMR signals of the guanine in the **chelates**-this downfield shift persists in monodentate N7 coordinated forms favored by protonation of the phosphate group at acid pH; and (c) characteristic changes in the shifts and coupling constants of the deoxyribose 1H NMR signals. This unusual **chelation** mode of binding has been characterized by NMR spectroscopy in only two previous studies. Interestingly, these studies involved other classes of metalloanticancer **agents**, namely Pt(II) and metallocene drugs. However, in these latter classes of drugs, only one isomer was possible. In the Ru derivatives studied here, the octahedral configuration leads to the possibility of diastereomers. After separation of the **chelates** by HPLC, the isomers were found to have nearly identical UV absorption spectra and a weak visible band at .apprx.410 nm. However, the CD spectra have bands that have

opposite signs but similar intensities and positions. Thus, the compound are isomers that differ principally by having an opposite chirality at ruthenium. Analysis of several types of experiments demonstrated that the isomers have the composition [RuIICl(H2O)(DSMO)2(5'-dGMP)]-. In **contrast** to the widely studied Pt(II) anticancer **agents**, the Ru drug does not readily bind to two 5'-dGMP at neutral pH. Thus, in addition to stereochemical differences between the octahedral Ru(II) and square-planar Pt(II) drugs, the Ru(II) compounds may not easily form the N7,N7 GpG crosslink characteristics of the **DNA** adducts formed by Pt anticancer drugs. Should the Ru(II) drugs form such a crosslink form, however, two diastereomers, with opposite chirality at Ru, are possible.

L33 ANSWER 4 OF 5 BIOSIS COPYRIGHT 1996 BIOSIS
ACCESSION NUMBER: 86:323585 BIOSIS
DOCUMENT NUMBER: BA82:47890
TITLE: INHIBITION OF EUGLENA-GRACILIS AND WHEAT GERM ZINC **RNA** POLYMERASES II BY 1 10 PHENANTHROLINE ACTING AS A **CHELATING AGENT**.
AUTHOR(S): MAZUS B; FALCHUK K H; VALLEE B L
CORPORATE SOURCE: CENTER BIOCHEM. BIOPHYSICAL SCI. MED., BRIGHAM AND WOMEN'S HOSP., HARVARD MED. SCH., BOSTON, MA 02115.
SOURCE: BIOCHEMISTRY 25 (10). 1986. 2941-2945. CODEN: BICHAW ISSN: 0006-2960
LANGUAGE: English
AB Copper complexes of 1,10-phenanthroline (OP-Cu) hydrolyze **DNA** [D'Aurora, V., Stern, A. M., & Sigman, D. S. (1978) Biochem. Biophys. Res. Commun. 80, 1025-1032; Marshall Pope, L., Reich, K. A., Graham, D. R., & Sigman, D. S. (1982) J. Biol, Chem. 257, 12121-12128]. This reaction has been studied to determine whether the 1,10-phenanthroline (OP) inhibition of the activity of **RNA** and **DNA** polymerases is the result of template hydrolysis or the **chelation** of a metal associated with and essential to the function of these enzymes. Addition of 4',6-diamino-2-phenylindole dihydrochloride (DAPI) to **DNA** generates a fluorescence signal with a linear increase of the intensity over a broad range of **DNA** concentrations from 0 to 100 .mu.g/mL. The progress of hydrolysis of **DNA** by DNase I or OP (2 mM) is monitored by the time-dependent decrease in DAPI-induced fluorescence. In the presence of OP, the rate of hydrolysis increases as the Cu2+ concentration in the reaction mixture arises from 10-8 to 10-5 M. The rate differs for each **nucleic acid** template used; hydrolysis of poly(dA-dT) > denatured **DNA** > double-stranded **DNA**. However, millimolar amounts of OP do not hydrolyze the template even in the presence of Cu2+ (10-6 M) when **DNA** is complexed with either Escherichia coli **DNA** polymerase I or Euglena gracilis or wheat germ **RNA** polymerase II. Under the same conditions, OP inhibits the activity of both varieties of **RNA** polymerase II with pKi's of 3.4 and 3.0, respectively. The addition of neocuproine from 10-5 to 10-3 M to **chelate** any Cu2+ present in the reaction mixture does not change this inhibition. In **contrast**, OP does not affect **DNA** polymerase I activity. Thus, OP inhibits enzyme activity of a complex of **RNA** polymerase with **nucleic acid** template by **chelation** of metal atoms essential for the function of these polymerases rather than by hydrolysis of their template. Zinc is the only enzymatically active metal associated with **RNA** polymerases. This functional role is confirmed further by the demonstration that these enzymes are also

inhibited by other **chelating agents** whose structures differ distinctively from that of OP: dipicolinic acid, 8-hydroxyquinoline, .alpha..alpha.'-bipyridyl, and 8-hydroxyquinoline-5-sulfonic acid.

L33 ANSWER 5 OF 5 BIOSIS COPYRIGHT 1996 BIOSIS
ACCESSION NUMBER: 85:390167 BIOSIS
DOCUMENT NUMBER: BA80:60159
TITLE: MODULATION OF TRANSFERRIN RECEPTOR EXPRESSION BY INHIBITORS OF **NUCLEIC-ACID** SYNTHESIS.
AUTHOR(S): HEDLEY D; RUGG C; MUSGROVE E; TAYLOR I
CORPORATE SOURCE: LUDWIG INST. CANCER RES., BLACKBURN BUILDING, UNIV. SYDNEY, SYDNEY, N.S.W. 2006, AUST.
SOURCE: J CELL PHYSIOL 124 (1). 1985. 61-66. CODEN: JCLLAX ISSN: 0021-9541
LANGUAGE: English
AB The effects of the Fe **chelator**, deferrioxamine on the expression of transferrin receptors (TfR) by CCRF-CEM human T-cell leukemia and B16 mouse melanoma cells growing in tissue culture were investigated. Deferrioxamine (DFOA) enhanced TfR expression when added in the dose range of 10-5-10-4 to CCRF-CEM cells, but was toxic to these cells; the lower concentrations produced a slowing of cell growth with a build up in S-phase, while higher concentrations caused cell death with a block at the G1/S-phase interface. These toxic effects are compatible with its previously reported inhibition of the non-heme-Fe containing (M2) subunit of ribonucleotide reductase. In marked **contrast**, DFOA caused the growth of B16 melanoma cells to arrest in G1, without loss of cloning efficiency, and resulted in a fall in TfR expression to .apprx. 50% of control values. The effects of DFOA on TfR expression were evidently linked to **DNA** synthesis rather than to a more generalized inhibition of Fe-dependent cellular processes. Inhibition of the M2 subunit of ribonucleotide reductase in CCRF-CEM cells with 5 .times. 10-5 M hydroxyurea, which is not an Fe **chelator**, also enhanced TfR expression, as did thymidine and cytosine arabinoside, which have different enzyme targets. By measuring cellular **DNA** and **RNA** content simultaneously, all of these **agents** evidently caused unbalanced growth, i.e., inhibited **DNA** synthesis more than **RNA** synthesis. In **contrast**, 6-thioguanine was more inhibitory to **RNA** synthesis; treatment with this drug caused a fall in TfR expresion. Although CCRF-CEM cells treated with DFOA show enhanced TfR expression, similar effects are also seen with other inhibitors of **DNA** synthesis, provided that **RNA** synthesis is allowed to continue. These results provide further evidence that the regulation of TfR expression by proliferating cells is specifically linked to **DNA** synthesis rather than to the Fe requirements of other cellular processes.

=> d l34 ibib ab 1-

L34 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 96071182 MEDLINE
TITLE: Role of **RNA** secondary structure of the iron-responsive element in translational regulation of ferritin synthesis.
AUTHOR: Kikinis Z; Eisenstein R S; Bettany A J; Munro H N
CORPORATE SOURCE: Division of Toxicology, Massachusetts Institute of Technology, Cambridge 02139, USA.
SOURCE: NUCLEIC ACIDS RESEARCH, (1995 Oct 25) 23 (20) 4190-5.

Journal code: O8L. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 9602

AB Iron regulates synthesis of the iron storage protein ferritin at the translational level through interaction between a stem-loop structure, the iron-responsive element (IRE), located in the 5'-untranslated region (5'-UTR) of ferritin mRNAs, and a protein, the iron regulatory protein (IRP). The role of IRE secondary structure in translational regulation of ferritin synthesis was explored by introducing ferritin constructs containing mutations in the IRE into Rat-2 fibroblasts. Our in vivo studies demonstrate that size and sequence of the loop within the IRE and the distance and/or spatial relationship of this loop to the bulged nucleotide region closest to the loop must be preserved in order to observe iron-dependent translation of ferritin mRNA. In **contrast**, changes in nucleotide sequence of the upper stem can be introduced without affecting translational regulation in vivo, as long as a stem can be formed. Our in vivo results suggest that only a very small variation in the affinity of interaction of IRP with IRE can be tolerated in order to maintain iron-dependent regulation of translation.

L34 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 91084467 MEDLINE
TITLE: Self-cleavage of hepatitis delta virus genomic strand **RNA** is enhanced under partially denaturing conditions.
AUTHOR: Rosenstein S P; Been M D
CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, North Carolina 27710..
CONTRACT NUMBER: GM-40689 (NIGMS)
SOURCE: BIOCHEMISTRY, (1990 Sep 4) 29 (35) 8011-6
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 9104

AB Self-cleavage of a polyribonucleotide containing an autocleaving sequence from the genomic strand of hepatitis delta virus was enhanced by conditions that destabilized **RNA** structure. Self-cleavage of the transcripts used in this study required Mg2+ (or another divalent cation), and in the absence of denaturants, maximum cleavage was observed at very low Mg2+ concentrations (0.05-0.1 mM). However, at 37 degrees C and in the presence of 2-10 mM Mg2+ the rate of cleavage was increased as much as 50-fold with the addition of urea to 5 M or formamide to 10 M. Cleavage was prevented by higher concentrations of the same reagents (9.5 M urea or 22.5 M formamide), presumably because a structure required for self-cleavage is disrupted by strongly denaturing conditions. In **contrast** to a previous report [Wu, H.-N., & Lai, M. M. C. (1989) Science 243, 652-654], we find that **chelating** Mg2+ with EDTA terminates the cleavage reaction without promoting measurable amounts of ligation of the cleavage products. The ability of denaturants to promote rapid self-cleavage in vitro raises the possibility that an unidentified factor could have a similar effect in vivo.

L34 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 90272648 MEDLINE
TITLE: Transferrin-polycation-mediated introduction of **DNA** into human leukemic cells: stimulation by **agents** that affect the survival of transfected **DNA** or modulate transferrin receptor levels.
AUTHOR: Cotten M; Langle-Rouault F; Kirlappos H; Wagner E; Mechtler K; Zenke M; Beug H; Birnstiel M L
CORPORATE SOURCE: Research Institute of Molecular Pathology, Vienna, Austria..
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Jun) 87 (11) 4033-7.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 9009
AB We have subverted a receptor-mediated endocytosis event to transport genes into human leukemic cells. By coupling the natural iron-delivery protein transferrin to the **DNA**-binding polycations polylysine or protamine, we have created protein conjugates that bind **nucleic acids** and carry them into the cell during the normal transferrin cycle [Wagner, E., Zenke, M., Cotten, M., Beug, H. & Birnstiel, M. L. (1990) Proc. Natl. Acad. Sci. USA 87, 3410-3414]. We demonstrate here that this procedure is useful for a human leukemic cell line. We enhanced the rate of gene delivery by (i) increasing the transferrin receptor density through treatment of the cells with the cell-permeable iron **chelator** desferrioxamine, (ii) interfering with the synthesis of heme with succinyl acetone treatment, or (iii) stimulating the degradation of heme with cobalt chloride treatment. Consistent with gene delivery as an endocytosis event, we show that the subsequent expression in K-562 cells of a gene included in the transported **DNA** depends upon the cellular presence of the lysosomotropic **agent** chloroquine. By **contrast**, monensin blocks "transferrinfection," as does incubation of the cells at 18 degrees C.

L34 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 86008502 MEDLINE
TITLE: Modulation of transferrin receptor expression by inhibitors of **nucleic acid** synthesis.
AUTHOR: Hedley D; Rugg C; Musgrove E; Taylor I
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (1985 Jul) 124 (1) 61-6.
Journal code: HNB. ISSN: 0021-9541.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 8601
AB We investigated the effects of the iron **chelator** desferrioxamine on the expression of transferrin receptors (TfR) by CCRF-CEM human T-cell leukaemia and B16 mouse melanoma cells growing in tissue culture. Desferrioxamine (DFOA) enhanced TfR expression when added in the dose range of 10(-5)-10(-4) to CCRF-CEM cells, but was toxic to these cells, the lower concentrations producing a

slowing of cell growth with a build up in S-phase, while higher concentrations caused cell death with a block at the G1/S-phase interface. These toxic effects are compatible with its previously reported inhibition of the non-haem iron containing (M2) subunit of ribonucleotide reductase. In marked **contrast**, DFOA caused the growth of B16 melanoma cells to arrest in G1, without loss of cloning efficiency, and resulted in a fall in TfR expression to approximately 50% of control values. These results suggested that the effects of DFOA on TfR expression were linked to **DNA** synthesis rather than to a more generalised inhibition of iron-dependent cellular processes. It was subsequently found that inhibition of the M2 subunit of ribonucleotide reductase in CCRF-CEM cells with 5 X 10(-5) M hydroxyurea, which is not an iron **chelator**, also enhanced TfR expression, as did thymidine and cytosine arabinoside, which have different enzyme targets. By measuring cellular **DNA** and **RNA** content simultaneously it was shown that all of these **agents** caused unbalanced growth, i.e., inhibited **DNA** synthesis more than **RNA** synthesis. In **contrast**, 6-thioguanine was more inhibitory to **RNA** synthesis, and treatment with this drug caused a fall in TfR expression. Thus, although CCRF-CEM cells treated with DFOA show enhanced TfR expression, similar effects are also seen with other inhibitors of **DNA** synthesis, provided that **RNA** synthesis is allowed to continue. These results provide further evidence that the regulation of TfR expression by proliferating cells is specifically linked to **DNA** synthesis rather than to the iron requirements of other cellular processes.

L34 ANSWER 5 OF 5 MEDLINE
ACCESSION NUMBER: 77022073 MEDLINE
TITLE: Euglena gracilis **DNA** dependent **RNA** polymerase II: a zinc metalloenzyme.
AUTHOR: Falchuk K H; Mazus B; Ulpino L; Vallee B L
SOURCE: BIOCHEMISTRY, (1976 Oct 5) 15 (20) 4468-75.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 7702

AB Zinc is essential for cellular proliferation. Zinc deficiency of Euglena gracilis results in arrest of cell division and deranges **nucleic acid** and protein metabolism pointing to a decisive role of zinc in transcription and translation. We have, therefore, investigated the role of zinc in the function of the **DNA**-dependent **RNA** polymerases of this organism. Two **RNA** polymerases from zinc sufficient organisms were purified first by affinity chromatography on a **DNA** cellulose column and subsequently separated on diethylaminoethyl (DEAE)-Sephadex A-25. The two fractions were characterized as polymerase I and II by their elution pattern from DEAE-Sephadex and sensitivity to alpha-amanitin. **RNA** polymerase II has a provisional molecular weight of 700 000 and contains an average of 2.2 g=atoms of zinc per mol of enzyme, but not Mn, Cu, or Fe, as measured by microwave emission spectroscopy. **Chelating agents**, such as 1,10-phenanthroline, 8-hydroxyquinoline, 8-hydroxyquinoline-5-sulfonic acid, and lomofungin, inhibit activity. In **contrast**, the nonchelating analogues, 1,7-and 4,7-phenanthroline, do not affect activity. Inhibition by 1,10-phenanthroline is instantaneous and fully reversible by

dilution. 1,10-Phenanthroline also inhibits **RNA** polymerase I, suggesting a role of zinc in its function. The demonstration that **RNA** polymerase II is a zinc enzyme indicates the involvement of zinc in eukaryotic **RNA** synthesis and serves as a further basis for the definition of the role of this element in eukaryotic cell growth, division, and differentiation.

=> d l35 ibib ab 1-

L35 ANSWER 1 OF 3 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90223840 EMBASE
TITLE: Transferrin-polycation-mediated introduction of **DNA** into human leukemic cells: Stimulation by **agents** that affect the survival of transfected **DNA** or modulate transferrin receptor levels.
AUTHOR: Cotten M.; Langle-Rouault F.; Kirlappos H.; Wagner E.; Mechtler K.; Zenke M.; Beug H.; Birnstiel M.L.
CORPORATE SOURCE: Research Institute of Molecular Pathology, Dr. Bohr-Gasse 7, 1030 Vienna, Austria
SOURCE: PROC. NATL ACAD. SCI. U. S. A., (1990) 87/11 (4033-4037).
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
AB We have subverted a receptor-mediated endocytosis event to transport genes into human leukemic cells. By coupling the natural iron-delivery protein transferrin to the **DNA**-binding polycations polylysine or protamine, we have created protein conjugates that bind **nucleic acids** and carry them into the cell during the normal transferrin cycle [Wagner, E., Zenke, M., Cotten, M., Beug, H. and Birnstiel, M.L. (1990) Proc. Natl. Acad. Sci. USA 87, 3410-3414]. We demonstrate here that this procedure is useful for a human leukemic cell line. We enhanced the rate of gene delivery by (i) increasing the transferrin receptor density through treatment of the cells with the cell-permeable iron **chelator** desferrioxamine, (ii) interfering with the synthesis of heme with succinyl acetone treatment, or (iii) stimulating the degradation of heme with cobalt chloride treatment. Consistent with gene delivery as an endocytosis event, we show that the subsequent expression in K-562 cells of a gene included in the transported **DNA** depends upon the cellular presence of the lysosomotropic **agent** chloroquine. By **contrast**, monensin blocks 'transferrinfection', as does incubation of the cells at 18.degree.C.

L35 ANSWER 2 OF 3 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89217293 EMBASE
TITLE: Novel diastereomers with opposite chirality at ruthenium formed by N7,.alpha.-PO4 **chelation** of 5'-dGMP to the antimetastatic **agent** trans-RuCl2(DMSO)4: NMR and CD evidence.
AUTHOR: Alessio E.; Xu Y.; Cauci S.; Mestroni G.; Quadrifoglio F.; Viglino P.; Marzilli L.G.
CORPORATE SOURCE: Department of Chemical Sciences, University of Trieste, 34127 Trieste, Italy
SOURCE: J. AM. CHEM. SOC., (1989) 111/18 (7068-7071).
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States

DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

AB A novel diastereometric pair of isomers was discovered in an initial study of the interaction of the antimetastatic **agent** trans-RuCl2(DMSO)4 with **nucleic acid** components. In particular, 5'-dGMP forms two products that have characteristic features clearly indicating that the guanine N7 and the .alpha.-phosphate group form a **chelate** to the metal center. These features include (a) a pronounced downfield shift of the 31P NMR signals of the **chelates**; (b) a downfield shift of the H8 1H NMR signals of the guanine in the **chelates** - this downfield shift persists in monodentate N7 coordinated forms favored by protonation of the phosphate group at acid pH; and (c) characteristic changes in the shifts and coupling constants of the deoxyribose 1H NMR signals. This unusual **chelation** mode of binding has been characterized by NMR spectroscopy in only two previous studies. Interestingly, these studies involved other classes of metalloanticancer **agents**, namely Pt(II) and metallocene drugs. However, in these latter classes of drugs, only one isomer was possible. In the Ru derivatives studied here, the octahedral configuration leads to the possibility of diastereomers. After separation of the **chelates** by HPLC, the isomers were found to have nearly identical UV absorption spectra and a weak visible band at .apprx.410 nm. However, the CD spectra have bands that have opposite signs but similar intensities and positions. Thus, the compounds are isomers that differ principally by having an opposite chirality at ruthenium. Analysis of several types of experiments demonstrated that the isomers have the composition [Ru(II)Cl(H2O)(DMSO)2(5'-dGMP)]-. In **contrast** to the widely studied Pt(II) anticancer **agents**, the Ru drug does not readily bind to two 5'-dGMP at neutral pH. Thus, in addition to stereochemical differences between the octahedral Ru(II) and square-planar Pt(II) drugs, the Ru(II) compounds may not easily form the N7,N7 GpG crosslink characteristic of the **DNA** adducts formed by Pt anticancer drugs. Should the Ru(II) drugs form such a crosslink form, however, two diastereomers, with opposite chirality at Ru, are possible.

L35 ANSWER 3 OF 3 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 85192640 EMBASE
TITLE: Modulation of transferrin receptor expression by inhibitors of **nucleic acid** synthesis.
AUTHOR: Hedley D.; Rugg C.; Musgrove E.; Taylor I.
CORPORATE SOURCE: Ludwig Institute for Cancer Research, Blackburn Building, University of Sydney, Sydney, NSW 2006, Australia
SOURCE: J. CELL. PHYSIOL., (1985) 124/1 (61-66).
CODEN: JCLLAX
COUNTRY: United States
LANGUAGE: English

AB We investigated the effects of the iron **chelator** desferrioxamine on the expression of transferrin receptors (TfR) by CCRF-CEM human T-cell leukaemia and B16 mouse melanoma cells growing in tissue culture. Desferrioxamine (DFOA) enhanced TfR expression when added in the dose range of 10-5-10-4 to CCRF-CEM cells, but was toxic to these cells, the lower concentrations producing a slowing of cell growth with a build up in S-phase, while higher concentrations caused cell death with a block at the G1/S-phase interface. These toxic effects are compatible with its previously

reported inhibition of the non-haem iron containing (M2) subunit of ribonucleotide reductase. In marked **contrast**, DFOA caused the growth of B16 melanoma cells to arrest in G1, without loss of cloning efficiency, and resulted in a fall in TfR expression to approximately 50% of control values. These results suggested that the effects of DFOA on TfR expression were linked to **DNA** synthesis rather than to a more generalised inhibition of iron-dependent cellular processes. It was subsequently found that inhibition of the M2 subunit of ribonucleotide reductase in CCRF-CEM cells with 5 x 10-5 M hydroxyurea, which is not an iron **chelator**, also enhanced TfR expression, as did thymidine and cytosine arabinoside, which have different enzyme target. By measuring cellular **DNA** and **RNA** content simultaneously it was shown that all of these **agents** caused unbalanced growth, i.e., inhibited **DNA** synthesis more than **RNA** synthesis. In **contrast**, 6-thioguanine was more inhibitory to **RNA** synthesis, and treatment with this drug caused a fall in TfR expression. Thus, although CCRF-CEM cells treated with DFOA show enhanced TfR expression, similar effects are also seen with other inhibitors of **DNA** synthesis, provided that **RNA** synthesis is allowed to continue. These results provide further evidence that the regulation of TfR expression by proliferating cells is specifically linked to **DNA** synthesis rather than to the iron requirements of other cellular processes.

```
=> s l42 and herpes
L46           0 FILE CAPLUS
L47           0 FILE BIOSIS
L48           0 FILE MEDLINE
L49           0 FILE EMBASE
L50          81 FILE USPATFULL

TOTAL FOR ALL FILES
L51          81 L42 AND HERPES

=> s l51 and poly amine?
L52           0 FILE CAPLUS
L53           0 FILE BIOSIS
L54           0 FILE MEDLINE
L55           0 FILE EMBASE
L56           2 FILE USPATFULL

TOTAL FOR ALL FILES
L57           2 L51 AND POLY AMINE?

=> d ibib ab 1-

L57  ANSWER 1 OF 2  USPATFULL
ACCESSION NUMBER:        89:56389  USPATFULL
TITLE:                   Method of effecting cellular uptake of molecules
INVENTOR(S):             Ryser, Hugues J. P., Concord, MA, United States
                         Shen, Wei-Chiang, Needham, MA, United States
PATENT ASSIGNEE(S):      The Trustees of Boston University, Boston, MA,
                         United States (U.S. corporation)

                           NUMBER      DATE
                         ------------ ------
PATENT INFORMATION:       US 4847240   890711
APPLICATION INFO.:        US 87-106129 871007  (7)
RELATED APPLN. INFO.:     Division of Ser. No. US 79-2368, filed on 10 Jan
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1979, now patented, Pat. No. US 4701521
Continuation-in-part of Ser. No. US 78-925075, filed on 17 Jul 1978, now abandoned
Continuation-in-part of Ser. No. US 78-869894, filed on 16 Jan 1978, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Phillips, Delbert R.
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 2218
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of effecting cellular uptake of molecules which are either excluded from cells or poorly transported into cells is disclosed wherein such molecules are covalently bonded to a cationic polymer which serves as a transport carrier to transport the molecules into cells.

L57 ANSWER 2 OF 2 USPATFULL
ACCESSION NUMBER: 87:73381 USPATFULL
TITLE: Method of effecting cellular uptake of molecules
INVENTOR(S): Ryser, Hugues J., Concord, MA, United States
Shen, Wei-Chiang, Needham, MA, United States
PATENT ASSIGNEE(S): The Trustees of Boston University, Boston, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4701521	871020
APPLICATION INFO.:	US 79-2368	790110 (6)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 78-925075, filed on 17 Jul 1978, now abandoned which is a continuation-in-part of Ser. No. US 78-869894, filed on 16 Jan 1978, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Phillips, Delbert R.
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 2169
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of effecting cellular uptake of molecules which are either excluded from cells or poorly transported into cells is disclosed wherein such molecules are covalently bonded to a cationic polymer which serves as a transport carrier to transport the molecules into cells.

=> s l51 and thymidine?
L58 0 FILE CAPLUS
L59 0 FILE BIOSIS
L60 0 FILE MEDLINE
L61 0 FILE EMBASE
L62 47 FILE USPATFULL

TOTAL FOR ALL FILES
L63 47 L51 AND THYMIDINE?06 COM

=> s l47 and kinase?
L64 0 FILE CAPLUS

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L65           0 FILE BIOSIS
L66           0 FILE MEDLINE
L67           0 FILE EMBASE
L68          59 FILE USPATFULL

TOTAL FOR ALL FILES
L69          59 L47 AND KINASE?

=> s l69 and protein?
L70           0 FILE CAPLUS
L71           0 FILE BIOSIS
L72           0 FILE MEDLINE
L73           0 FILE EMBASE
L74          58 FILE USPATFULL

TOTAL FOR ALL FILES
L75          58 L69 AND PROTEIN?

=> s l51 and herpes thymidine kinase?
L76           0 FILE CAPLUS
L77           0 FILE BIOSIS
L78           0 FILE MEDLINE
L79           0 FILE EMBASE
L80           2 FILE USPATFULL

TOTAL FOR ALL FILES
L81           2 L51 AND HERPES THYMIDINE KINASE?

=> d ibib ab 1-

L81  ANSWER 1 OF 2  USPATFULL
ACCESSION NUMBER:        95:62634  USPATFULL
TITLE:                   Host cells transformed with the E. coli
                         glucoronide permease gene
INVENTOR(S):             Jefferson, Richard A., Canberra Act, Australia
PATENT ASSIGNEE(S):      Cambia Biosystems, L.L.C., New York, NY, United
                         States (U.S. corporation)

                            NUMBER      DATE
                         ------------ ------
PATENT INFORMATION:      US 5432081   950711
APPLICATION INFO.:       US 93-138546 931015  (8)
RELATED APPLN. INFO.:    Division of Ser. No. US 89-447976, filed on 8 Dec
                         1989, now patented, Pat. No. US 5268463, issued
                         on 7 Dec 1993 which is a continuation-in-part of
                         Ser. No. US 88-264586, filed on 31 Oct 1988, now
                         abandoned which is a continuation-in-part of Ser.
                         No. US 87-119102, filed on 10 Nov 1987, now
                         abandoned

                            NUMBER      DATE
                         ------------ ------
PRIORITY INFORMATION:    GB 86-26862  861111
                         GB 87-25402  871029
DOCUMENT TYPE:           Utility
PRIMARY EXAMINER:        Schwartz, Richard A.
ASSISTANT EXAMINER:      LeGuyader, J.
LEGAL REPRESENTATIVE:    Pennie & Edmonds
NUMBER OF CLAIMS:        6
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      29 Drawing Figure(s); 24 Drawing Page(s)
```

LINE COUNT: 3791
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the .beta.-glucuronidase (GUS) gene fusion system, and to the cloning and characterization of the .beta.-glucuronidase and glucuronide permease genes of Escherichia coli. It is based on the surprising discovery that gene fusions comprising the .beta.-glucuronidase gene may be effectively expressed in a wide variety of organisms to produce active .beta.-glucuronidase enzyme. Because of the abundance and availability of useful substrates for .beta.-glucuronidase enzyme, GUS gene fusions may serve as a superior reporter gene system as well as an effective means of altering cellular phenotype. In conjunction with recombinant glucuronide permease, which may be used to render host cells permeable to .beta.-glucuronidase substrates, the GUS gene fusion system offers almost unlimited applications in the fields of plant and animal genetic engineering.

L81 ANSWER 2 OF 2 USPATFULL
ACCESSION NUMBER: 93:102875 USPATFULL
TITLE: Plant promoter .alpha.-glucuronidase gene construct
INVENTOR(S): Jefferson, Richard A., 9, The Cobbles Wingate Way, Trumpington, Cambridge, England CB2 2HA

	NUMBER	DATE
PATENT INFORMATION:	US 5268463	931207
APPLICATION INFO.:	US 89-447976	891208 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 87-119102, filed on 10 Nov 1987, now abandoned And Ser. No. US 88-264586, filed on 31 Oct 1988, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 86-26862	861111

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Schwartz, Richard A.
ASSISTANT EXAMINER: LeGuyader, John
LEGAL REPRESENTATIVE: Pennie & Edmonds
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 29 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT: 3598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the .beta.-glucuronidase (GUS) gene fusion system, and to the cloning and characterization of the .beta.-glucuronidase and glucuronide permease genes of Escherichia coli. It is based on the surprising discovery that gene fusions comprising the .beta.-glucuronidase gene may be effectively expressed in a wide variety of organisms to produce active .beta.-glucuronidase enzyme. Because of the abundance and availability of useful substrates for .beta.-glucuronidase enzyme, GUS gene fusions may serve as a superior reporter gene system as well as an effective means of altering cellular phenotype. In conjunction with recombinant glucuronide permease, which may be used to render host cells permeable to .beta.-glucuronidase substrates, the GUS gene fusion system offers almost unlimited applications in the fields of plant and animal genetic engineering.

9/16/96

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Enter terminal type or "M" for menu - KSR

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TERMINAL (ENTER 1, 2, 3, 4, OR ?):3

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  *    10 Sep. 1996 for U.S. Current Classification data.               *
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  *  including any warranty of marketability of fitness for a           *
  *  particular purpose; nor assumes any legal liability or             *
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  *      Saturday, Sunday, Holidays: 8:30am - 5:00 pm                   *
  *                                                                     *
  *    The Help Desk staff at this number will handle all APS           *
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  *            6:30am - 9:00pm Monday through Friday                    *
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  *      and New Year's Day.                                            *
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FILE 'USPAT' ENTERED AT 09:26:05 ON 16 SEP 96

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=> s 424/1.11,1.65,1.73,9.1,9.3,9.34/ccls
            54 424/1.11/CCLS
           182 424/1.65/CCLS
            60 424/1.73/CCLS
            74 424/9.1/CCLS
            52 424/9.3/CCLS
            87 424/9.34/CCLS
L1         451 424/1.11,1.65,1.73,9.1,9.3,9.34/CCLS
                 ((424/1.11 OR 424/1.65 OR 424/1.73 OR 424/9.1 OR 424/9.3
OR
                 424/9.34)/CCLS)

=> s 536/22.1,25.6,27.1,26.1/ccls
           234 536/22.1/CCLS
            38 536/25.6/CCLS
            51 536/27.1/CCLS
            34 536/26.1/CCLS
L2         339 536/22.1,25.6,27.1,26.1/CCLS
                 ((536/22.1 OR 536/25.6 OR 536/27.1 OR 536/26.1)/CCLS)

=> 530/300,324,325,326,327,328,329,330/ccls
'530' IS NOT A RECOGNIZED COMMAND

=> s 530/300,324,325,326,327,328,329,330/ccls
           421 530/300/CCLS
           947 530/324/CCLS
           273 530/325/CCLS
           571 530/326/CCLS
           521 530/327/CCLS
           682 530/328/CCLS
           552 530/329/CCLS
           763 530/330/CCLS
L3        2700 530/300,324,325,326,327,328,329,330/CCLS
                 ((530/300 OR 530/324 OR 530/325 OR 530/326 OR 530/327 OR
530
                 /328 OR 530/329 OR 530/330)/CCLS)


=> s 534/10,11,12,13,14,15,16/ccls
           509 534/10/CCLS
           391 534/11/CCLS
           171 534/12/CCLS
           290 534/13/CCLS
           460 534/14/CCLS
           549 534/15/CCLS
           418 534/16/CCLS
L4        1539 534/10,11,12,13,14,15,16/CCLS
                 ((534/10 OR 534/11 OR 534/12 OR 534/13 OR 534/14 OR 534/1
5 O
                 R 534/16)/CCLS)

=> s l1 or l2 or l3 or l4
L5        4874 L1 OR L2 OR L3 OR L4

=> s l5 and nucleic acid?
         10375 NUCLEIC
        400879 ACID?
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         10295 NUCLEIC ACID?
                 (NUCLEIC(W)ACID?)
L6         749 L5 AND NUCLEIC ACID?

=> s l6 and (contrast? or imag?)
        228209 CONTRAST?
        268777 IMAG?
L7         341 L6 AND (CONTRAST? OR IMAG?)

=> s l7 and (dna or rna or deoxy ribo? or ribo nucleic?)
         15750 DNA
          8386 RNA
          4154 DEOXY
         11321 RIBO?
            83 DEOXY RIBO?
                 (DEOXY(W)RIBO?)
           283 RIBO
         10388 NUCLEIC?
             9 RIBO NUCLEIC?
                 (RIBO(W)NUCLEIC?)
L8         309 L7 AND (DNA OR RNA OR DEOXY RIBO? OR RIBO NUCLEIC?)

=> s l8 and chelat?
         23029 CHELAT?
L9          64 L8 AND CHELAT?

=> s l9 and (cancer? or tumour? or tumor? or neoplas?)
         17452 CANCER?
          1482 TUMOUR?
         16258 TUMOR?
          4138 NEOPLAS?
L10         38 L9 AND (CANCER? OR TUMOUR? OR TUMOR? OR NEOPLAS?)

=> d pn ti ab 1-
US PAT NO:      5,552,529 [IMAGE AVAILABLE]          L10: 1 of 38
TITLE:          Autoantigen, pinch

ABSTRACT:
A novel autoantigenic polypeptide, PINCH, polynucleotides and antibodies
that bind to PINCH are provided. A method for removing autoantibodies
that bind to an epitope contained in PINCH from a sample, such as blood,
and a method of treating autoimmune disorders associated with
autoantibodies that bind an epitope in PINCH are also provided.
US PAT NO:      5,550,034 [IMAGE AVAILABLE]          L10: 2 of 38
TITLE:          Apolipoprotein B mRNA editing protein compositions and
                  methods

ABSTRACT:
The present invention provides a protein that edits apo B **RNA**. A
polynucleotide that comprises a **DNA** sequence that encodes an apo B
**RNA** editing protein and an expression vector comprising such a
polynucleotide are also provided. Processes for producing an apo B
**RNA** editing protein, editing apo B **RNA** and altering apo B protein
production are also provided.
US PAT NO:      5,541,287 [IMAGE AVAILABLE]          L10: 3 of 38
TITLE:          Pretargeting methods and compounds

ABSTRACT:
Methods, compounds, compositions and kits that relate to pretargeted
delivery of diagnostic and therapeutic agents are disclosed. In
particular, methods for radiometal labeling of biotin, as well as related
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compounds, are described. Articles of manufacture useful in pretargeting methods are also discussed.

US PAT NO: 5,539,082 [IMAGE AVAILABLE] L10: 4 of 38
TITLE: Peptide **nucleic** **acids**

ABSTRACT:
A novel class of compounds, known as peptide **nucleic** **acids**, bind complementary ssDNA and **RNA** strands more strongly than a corresponding **DNA**. The peptide **nucleic** **acids** generally comprise ligands such as naturally occurring **DNA** bases attached to a peptide backbone through a suitable linker.

US PAT NO: 5,534,426 [IMAGE AVAILABLE] L10: 5 of 38
TITLE: Oncoprotein protein kinase

ABSTRACT:
An isolated polypeptide (JNK) characterized by having a molecular weight of 46kD as determined by reducing SDS-PAGE, having serine and threonine kinase activity, phosphorylating the c-Jun N-terminal activation domain and polynucleotide sequences and method of detection of JNK.

US PAT NO: 5,532,122 [IMAGE AVAILABLE] L10: 6 of 38
TITLE: Quantitation of gamma and x-ray emitting isotopes

ABSTRACT:
For isotopes decaying by capture of an inner shell electron by the nucleus, coincident emission of X-ray and gamma photons may occur. The X-ray results from the drop of an outer shell electron to fill the S shell. The gamma results from the transition of the excited daughter nucleus to a lower energy state. The invention disclosed is a Coincident Gamma and X-ray Detector (CGXD) which achieves extraordinary background rejection by a synergistic combination of coincident counting and other background suppression measures. Whereas the background registered by single gamma counters is of the order of 20-40 counts per minute, a CGXD optimized for the electron capture radioisotope I.sup.125 has a background of about one count per day.

US PAT NO: 5,527,885 [IMAGE AVAILABLE] L10: 7 of 38
TITLE: Bifunctional isothiocyanate derived thiocarbonyls as ligands for metal binding

ABSTRACT:
This invention relates to **chelating** agents useful for coupling metal ions to biologically active molecules. In particular, isothiocyanate derived thiocarbonyls for **chelating** metals such as technetium are provided that can be conjugated to a targeting molecule such as an antibody, a peptide or a protein.

US PAT NO: 5,527,524 [IMAGE AVAILABLE] L10: 8 of 38
TITLE: Dense star polymer conjugates

ABSTRACT:
Dense star polymer conjugates which are composed of at least one dendrimer in association with at least one unit of a carried agricultural, pharmaceutical, or other material have been prepared. These conjugates have particularly advantageous properties due to the unique characteristics of the dendrimer.

US PAT NO: 5,521,288 [IMAGE AVAILABLE] L10: 9 of 38
TITLE: CD28IG fusion protein

ABSTRACT:
The invention identifies the B7 antigen as a ligand that is reactive with the CD28 receptor on T cells. Fragments and derivatives of the B7 antigen and CD28 receptor, including fusion proteins having amino acid sequences corresponding to the extracellular domains of B7 or CD28 joined to amino

acid sequences encoding portions of human immunoglobulin C.gamma.1, are described. Methods are provided for using B7 antigen, its fragments and derivatives, and the CD28 receptor, its fragments and derivatives, as well as antibodies and other molecules reactive with B7 antigen and/or the CD28 receptor, to regulate CD28 positive T cell responses, and immune responses mediated by T cells. The invention also includes an assay method for detecting ligands reactive with cellular receptors mediating intercellular adhesion.

US PAT NO: 5,518,888 [IMAGE AVAILABLE] L10: 10 of 38
TITLE: ST receptor binding compounds and methods of using the same

ABSTRACT:
Conjugated compounds which comprises an ST receptor binding moiety and a radiostable active moiety are disclosed. Pharmaceutical compositions comprising a pharmaceutically acceptable carrier or diluent, and a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radioactive active moiety are disclosed. Methods of treating an individual suspected of suffering from metastasized colorectal **cancer** comprising the steps of administering to said individual a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent, and a therapeutically effective amount of a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radiostable active moiety are disclosed. Methods of radioimaging metastasized colorectal **cancer** cells comprising the steps of first administering to an individual suspected of having metastasized colorectal **cancer** cells, a pharmaceutical composition that comprises a pharmaceutically acceptable carrier or diluent, and conjugated compound that comprises an ST receptor binding moiety and a radioactive active moiety wherein the conjugated compound is present in an amount effective for diagnostic use in humans suffering from colorectal **cancer** and then detecting the localization and accumulation of radioactivity in the individual's body are disclosed.

US PAT NO: 5,457,183 [IMAGE AVAILABLE] L10: 11 of 38
TITLE: Hydroxylated texaphyrins

ABSTRACT:
A method of using texaphyrins as radiosensitizers. Advantageous properties of texaphyrins for use as a radiosensitizer include i) a low redox potential which allows radiation induced solvated electrons to flow to texaphyrin rather than neutralizing hydroxyl radicals, allowing the hydroxyl radicals to cause cellular damage, ii) a relatively stable texaphyrin radical which, nevertheless, reacts readily to covalently modify neighboring molecules causing further cellular damage, and iii) intrinsic biolocalization and indifference to the presence of O.sub.2 which allow texaphyrin to be particularly effective for treating the hypoxic areas of solid **tumors**. Sensitizer enhancement ratios of 1.62 and 2.2 were achieved at 20 .mu.M and 80 .mu.M gadolinium-texaphyrin, respectively, with a mouse leukemia cell line. Methods of treatment for an individual having a **tumor** include the use of a texaphyrin as a radiosensitizer and as an agent for photodynamic **tumor** therapy, or the use of a texaphyrin for internal and for external ionizing radiation. New water soluble hydroxy-substituted texaphyrins are described.

US PAT NO: 5,449,761 [IMAGE AVAILABLE] L10: 12 of 38
TITLE: Metal-binding targeted polypeptide constructs

ABSTRACT:
This invention relates to the preparation and use of novel open-chain or cyclic polypeptide constructs in which two or more polypeptide chains, in an open-chain construct, or one or more chains, in a cyclic construct,

are chemically derivatized such that the resulting construct exhibits both metal-binding capability and tissue-, organ- or cell-targeting selectivity. In particular, the polypeptide constructs of the present invention comprise compounds of the formula (I): ##STR1## in which, "B" is a hydrocarbon backbone, "P" is a polypeptide capable of targeting particular cells, tissues or organs of the body, "A" may be the group --NR'--NR"-- or the group --NR'--NR"--L-- in which L may be an aliphatic r salt thereof which is
spectroscopically or photoactively determinable when bound to **DNA** having the formula ##STR1## wherein M is a suitable transition metal and each of R.sub.1, R.sub.2 and R.sub.3 is ethylenediamine or a substituted derivative thereof, bipyridine or a substituted derivative thereof, phenanthroline or a substituted derivative thereof, diazfluorene-9-one or a substituted derivative thereof, phenanthrenequinonediimine or a substituted derivative thereof; wherein R.sub.1, R.sub.2 and R.sub.3 are bound to M by coordination bonds wherein R.sub.1 and R.sub.2 are the same and both are different from R.sub.3. The invention also concerns a method of labeling **DNA** with the coordination complex, a **DNA** molecule labeled with the coordination complex, a method of selectively labeling **DNA** conformation with the coordination complex and a method of detecting the presence of a conformation present in a double stranded **DNA**.

US PAT NO: 5,434,058 [IMAGE AVAILABLE] L10: 14 of 38
TITLE: Apolipoprotein B MRNA editing protein compositions and methods

ABSTRACT:
The present invention provides a protein that edits apo B **RNA**. A polynucleotide that comprises a **DNA** sequence that encodes an apo B **RNA** editing protein and an expression vector comprising such a polynucleotide are also provided. Processes for producing an apo B **RNA** editing protein, editing apo B **RNA** and altering apo B protein production are also provided.

US PAT NO: 5,420,245 [IMAGE AVAILABLE] L10: 15 of 38
TITLE: Tetrapeptide-based inhibitors of farnesyl transferase

ABSTRACT:
Disclosed are methods and compositions for the identification, characterization and inhibition of mammalian farnesyl protein transferases, enzymes involved in the farnesylation of various cellular proteins, including **cancer** related ras proteins such as p21.sup.ras.- One farnesyl protein transferase which is disclosed herein exhibits a molecular weight of between about 70,000 and about 100,000 upon gel exclusion chromatography. Also disclosed are methods and compositions for the preparation of farnesyl transferase by recombinant means, following of proteins such as p21.sup.ras. Also disclosed is a families of compounds which act either as false substrates for the enzyme or as pure inhibitors and can therefore be employed for inhibition of the enzyme. The most potent inhibitors are ones in which phenylalanine occurs at the third position of a tetrapeptide whose amino terminus is cysteine.

US PAT NO: 5,420,244 [IMAGE AVAILABLE] L10: 16 of 38
TITLE: Methods and compositions for diagnosing HTLV-I associated myelopathy and adult T-cell leukemia

ABSTRACT:
The invention provides antigenic peptides derived from immunodominant epitopes of the HTLV-I tax or rex proteins that are immunoreactive with antibodies associated with disease in HTLV-I infected subjects. More specifically, the invention provides antigenic peptides consisting essentially of the amino acid sequences defined in the sequence listing by SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7 and 8 and antigenic fragments thereof.

The invention provides a method of diagnosing HTLV-I associated myelopathy (HAM) or a predisposition thereto, comprising the steps of: (a) contacting an antibody containing sample from the subject with a detectable amount of a peptide of the invention or an antigenic fragment thereof; and (b) detecting the reaction of the peptide with an antibody in the sample, the reaction indicating HTLV-I associated myelopathy or a predisposition thereto. The invention also provides a method of diagnosing adult T-cell leukemia or a predisposition thereto in a subject, comprising the steps of: (a) contacting an antibody containing sample from the subject with a detectable amount of the peptide of SEQ ID NO: 1; and (b) detecting the reaction of the peptide with an antibody in the sample, the reaction indicating adult T-cell leukemia or predisposition thereto.

US PAT NO: 5,416,192 [IMAGE AVAILABLE] L10: 17 of 38
TITLE: Epithelins: novel cysteine-rich growth modulating proteins

ABSTRACT:
A novel family of growth regulatory proteins termed "epithelins" are described. The epithelins comprise several distinct members sharing significant structural homology. Two members of the epithelin family, epithelin 1 and epithelin 2, have been purified from natural sources. In addition, cDNA and PCR clones encoding mature and precursor epithelins from various chordate sources have been obtained and sequenced, including the complete human, mouse and rat epithelin precursors. The recombinant expression of rat epithelin precursor and mature forms is described. Purified epithelin 1 is a bifunctional growth regulator, capable of stimulating the growth of some cell types while inhibiting the growth of others. Purified epithelin 2 is functionally similar to epithelin 1 with respect to growth inhibitory bioactivity. In **contrast**, however, epithelin 2 is apparently not capable of eliciting the growth stimulatory activity characteristic of epithelin 1 and, in fact, antagonizes this epithelin 1 activity.

US PAT NO: 5,373,093 [IMAGE AVAILABLE] L10: 18 of 38
TITLE: Macrocyclic complexes of yttrium, the lanthanides and the actinides having peripheral coupling functionalities

ABSTRACT:
Functionalized water soluble macrocyclic complexes of lanthanide, actinide and yttrium ions were obtained by metal templated, Schiff-base, cyclic condensation of: (1) a functionalized 1,2-diaminoethane and a dicarbonyl compound selected from the group consisting of 2,6-dicarbonylpyridine, 2,6-diformylpyridine, 2,5-dicarbonylfuran, 2,5-diformylfuran, 2,5-dicarbonylthiophene and 2,5-diformylthiophene; or (2) 1,2-diaminoethane and a ring-substituted heterocyclic dicarbonyl compound selected from a group consisting of substituted 2,6-dicarbonylpyridine, substituted 2,6-diformylpyridine, substituted 2,5-dicarbonylfuran, substituted 2,5-diformylfuran; substituted 2,5-dicarbonyl thiophene, and substituted 2,5-diformylthiophene. Coordination complexes thus formed are kinetically stable in dilute aqueous solution. They are further reacted, or coupled, through a substituent on the 1,2-diaminoethane or on the pyridine, furan, or thiophene moieties, to one of the following: proteinaceous materials, polysaccharides, other biologically compatible macromolecules or bridging molecules which, can be further reacted or coupled to the above mentioned substrates. These macrocyclic complexes are suitable in the preparation of reporter molecules and for magnetic resonance, radiation **imaging** and radiation therapy.

US PAT NO: 5,362,629 [IMAGE AVAILABLE] L10: 19 of 38
TITLE: Detection of immunosuppressants

ABSTRACT:

A method of evaluating the immunosuppressive activity of a compound including contacting the compound with calcineurin and determining the ability of the compound to bind to the calcineurin. The ability to bind to the calcineurin is positively correlated to the immunosuppressive activity of the compound.

US PAT NO: 5,350,671 [IMAGE AVAILABLE] L10: 20 of 38
TITLE: HCV immunoassays employing C domain antigens

ABSTRACT:
Immunoassays for the detection of antibodies to HCV are provided which employ "C" domain antigens. Immunoassay kits comprising such antigens are also provided.

US PAT NO: 5,346,670 [IMAGE AVAILABLE] L10: 21 of 38
TITLE: Phthalocyanine and tetrabenztriazaporphyrin reagents

ABSTRACT:
Red-shifted, water-soluble, fluorescent, monomerically-tetherable derivatives having the formula: ##STR1## wherein, M represents either H.sub.2 or is selected from among the following metals: aluminum, silicon, phosphorus, gallium, germanium, cadmium, scandium, magnesium, tin, and zinc. Each R.sub.1 is independently selected from --XYW, --YW, and --W. X represents either a carbon, or heteroatom selected from among oxygen, nitrogen, sulfur, phosphorus, silicon, and selenium; Y represents a linking group; and W represents a water solubilizing group. The substituent R.sub.2 is selected from among --A, --Y'A, --XA, and --XY'A, where A denotes a biological entity such as an antibody, antibody fragment, nucleotide, **nucleic** **acid** probe, antigen, oligonucleotide, deoxynucleotide, dideoxynucleotide, avidin, streptavidin or membrane probe, or R.sub.2 is a reactive or activatable group suitable for conjugating to a biological entity. Y' is a linking group that tethers the biological entity to the phthalocyanine or tetrabenztriazaporphyrin macrocycle. Z is either a nitrogen atom or a carbon substituted with hydrogen, alkyl, aryl, or aralkyl groups. Z may also be attached to R.sub.2. Also disclosed are derivatives of the compounds of the above Formula in which 1-4 of the benzo ring(s) contain 1 or 2 N atoms. Methods of sequencing **DNA** and detecting analytes, including cells, using these derivatives are disclosed, as are kits for carrying out assays for the analytes and flow cytometry. Methods of detecting **DNA** using cationic compounds of the above Formula, wherein R.sub.2 =R.sub.1 and W=-N.sup.+ D.sub.1 D.sub.2 D.sub.3 are also disclosed. Further, compounds containing Tc, Gd, etc. as the metal in the above Formula may be used for **imaging** or therapy.

US PAT NO: 5,328,840 [IMAGE AVAILABLE] L10: 22 of 38
TITLE: Method for preparing targeted carrier erythrocytes

ABSTRACT:
The present invention provides new compounds and methods for promoting platelet aggregation, and controlling bleeding. The present invention is based on the surprising discovery that erythrocytes conjugated to certain peptides and polypeptides containing an R-G-D (Arg-Gly-Asp) sequence (collectively termed herein "RGD peptides") according to the invention, selectively bind to activated platelets but not to unactivated platelets. In recognition of the dual nature of the derivatized erythrocytes, they are termed herein "thrombo-erythrocytes". The thrombo-erythrocytes have no significant change in their rheological properties. In a preferred aspect, the thrombo-erythrocytes have the majority of RGD peptide cross-linked specifically to glycophorin A and glycophorin B on the surface of the erythrocyte. In the thrombo-erythrocytes of the invention, preferably, the N-terminal Arg of the R-G-D sequence should be spaced within 9-50 Angstroms, more preferably 10-40 Angstroms, and most preferably 11-25 Angstroms, from the erythrocyte protein to which the RGD

peptide is conjugated. The invention is further directed to erthrocytes modified by replacement of their intracellular contents with a composition comprising a label or agent. Such modified erythrocytes are termed herein "carrier erythrocytes". The carrier erythrocytes have use in delivery of such labels or biologically active agents to specific tissues by conjugation to a targeting agent.

US PAT NO: 5,326,856 [IMAGE AVAILABLE] L10: 23 of 38
TITLE: Bifunctional isothiocyanate derived thiocarbonyls as ligands for metal binding

ABSTRACT:
This invention relates to **chelating** agents useful for coupling metal ions to biologically active molecules. In particular, isothiocyanate derived thiocarbonyls for **chelating** metals such as technetium are provided that can be conjugated to a targeting molecule such as an antibody, a peptide or a protein.

US PAT NO: 5,317,011 [IMAGE AVAILABLE] L10: 24 of 38
TITLE: Cloning and expression of a variant gene of platelet factor 4 and compositions thereof to modulate immune responses

ABSTRACT:
The present invention provides for the purification from native sources or the cloning and expression of a variant form of platelet factor 4 and also provides recombinant **DNA** vectors and methods for the expression and recovery of the platelet factor 4 variant. Also provided are compositions and methods for modulating immune responses in mammals comprising immunomodulating effective amounts of platelet factor 4 variant.

US PAT NO: 5,312,810 [IMAGE AVAILABLE] L10: 25 of 38
TITLE: Method and compositions for making ACSF and ACSF antagonists

ABSTRACT:
Compositions comprising the C-terminal portion of adenylate cyclase stimulating factor (ACSF) are useful for making ACSF-specific antisera.

US PAT NO: 5,266,683 [IMAGE AVAILABLE] L10: 26 of 38
TITLE: Osteogenic proteins

ABSTRACT:
Disclosed are (1) osteogenic devices comprising a matrix containing substantially pure natural-sourced mammalian osteogenic protein; (2) **DNA** and amino acid sequences for novel polypeptide chains useful as subunits of dimeric osteogenic proteins; (3) vectors carrying sequences encoding these novel polypeptide chains and host cells transfected with these vectors; (4) methods of producing these polypeptide chains using recombinant **DNA** technology; (5) antibodies specific for these novel polypeptide chains; (6) osteogenic devices comprising these recombinantly produced proteins in association with an appropriate carrier matrix; and (7) methods of using the osteogenic devices to mimic the natural course of endochondral bone formation in mammals.

US PAT NO: 5,241,060 [IMAGE AVAILABLE] L10: 27 of 38
TITLE: Base moiety-labeled detectable nucleatide

ABSTRACT:
The present invention provides nucleotides and polynucleotides which are chemically modified or labeled so as to be capable of ready detection when attached to and/or incorporated in **nucleic** **acid** material. More particularly, this invention provides a nucleotide having the formula

PM-SM-BASE-Sig
wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a pyrimidine, purine or 7-deazapurine moiety. PM is attached at the 3' or the 5' position of SM when the nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when the nucleotide is a ribonucleotide. BASE is attached to the 1' position of SM from the N.sup.1 position when BASE is a pyrimidine or the N.sup.9 position when BASE is a purine or a 7-deazapurine. Sig is a detectable moiety that is covalently attached to BASE at a position other than the C.sup.5 position when BASE is a pyrimidine, at a position other than the C.sup.8 position when BASE is a purine and at a position other than the C.sup.7 position when BASE is a 7-deazapurine.

US PAT NO: 5,227,474 [IMAGE AVAILABLE] L10: 28 of 38
TITLE: Bifunctional **chelating** agents

ABSTRACT:
The present invention provides bifunctional **chelating** agents comprising a unique substrate reactive moiety incorporated into a carboxymethyl arm of a polyaminopolycarboxylate **chelating** framework capable of forming stable complexes with metal ions.

US PAT NO: 5,227,469 [IMAGE AVAILABLE] L10: 29 of 38
TITLE: Platelet aggregation inhibitors from the leech

ABSTRACT:
A composition of matter derived from hematophagous leech comprising specified purified amino acid sequences represented by the general formula:

CXXXRGDXXXXC(Seq. ID No. 11)
and capable of functioning as an antithrombotic by inhibiting the binding of fibrinogen to the platelet glycoprotein II.sub.b III.sub.a (GP II.sub.b III.sub.a), a fibrinogen receptor. Methods for the purification of amino acid sequences from leeches, and particularly from leeches of the genus Macrobdella and Placobdella. are provided. Isolated **nucleic** **acid** sequences encoding these amino acid sequences; an expression vector containing the isolated **nucleic** **acid**; and a cell containing the expression vector are also described. A process for chemical synthesis of the amino acid sequences and a method for reducing platelet aggregation in a mammal by administering a composition containing the amino acid sequences to the mammal in a pharmaceutically effective amount are provided.

US PAT NO: 5,218,092 [IMAGE AVAILABLE] L10: 30 of 38
TITLE: Modified granulocyte-colony stimulating factor polypeptide with added carbohydrate chains

ABSTRACT:
A polypeptide or glycosylated polypeptide with at least one new carbohydrate chain produced by means of recombinant **DNA** technique, which has protease resistance and thermal stability and is expected to have longer lifetime in blood than those of a naturally-occurring form.

US PAT NO: 5,196,510 [IMAGE AVAILABLE] L10: 31 of 38
TITLE: Molecular recognition units

ABSTRACT:
A system or method for identifying and/or designing novel peptides and polypeptides comprising an amino acid sequence which mimics the molecular recognition site of either (a) a macromolecule such as an immunoglobulin, an enzyme, a receptor protein, a lectin or other binding protein or (b) a small molecule or a small region of a large molecule which functions as a ligand and is recognized and binds specifically to a macromolecule is disclosed. Novel peptides and polypeptides as well as conjugates of the

peptides and polypeptides are also disclosed. Applications for use of the peptides, polypeptides and conjugates in a wide range of fields such as biomedicine; biological control and pest regulation; agriculture; cosmetics; environmental control and waste management; chemistry; catalysis; nutrition and food industries; military uses; climate control, etc. are disclosed.

US PAT NO: 5,091,513 [IMAGE AVAILABLE] L10: 32 of 38
TITLE: Biosynthetic antibody binding sites

ABSTRACT:
Disclosed are a family of synthetic proteins having affinity for a preselected antigen. The proteins are characterized by one or more sequences of amino acids constituting a region which behaves as a biosynthetic antibody binding site (BABS). The sites comprise 1) non-covalently associated or disulfide bonded synthetic V.sub.H and V.sub.L dimers, 2) V.sub.H -V.sub.L or V.sub.L -V.sub.H single chains wherein the V.sub.H and V.sub.L are attached by a polypeptide linker, or 3) individuals V.sub.H or V.sub.L domains. The binding domains comprise linked CDR and FR regions, which may be derived from separate immunoglobulins. The proteins may also include other polypeptide sequences which function e.g., as an enzyme, toxin, binding site, or site of attachment to an immobilization media or radioactive atom. Methods are disclosed for producing the proteins, for designing BABS having any specificity that can be elicited by in vivo generation of antibody, and for producing analogs thereof.

US PAT NO: 5,057,302 [IMAGE AVAILABLE] L10: 33 of 38
TITLE: Bifunctional **chelating** agents

ABSTRACT:
The present invention provides bifunctional **chelating** agents comprising a unique substrate reactive moiety incorporated into a carboxymethyl arm of a polyaminopolycarboxylate **chelating** framework capable of forming stable complexes with metal ions.

US PAT NO: 4,927,923 [IMAGE AVAILABLE] L10: 34 of 38
TITLE: Macropolycyclic rare earth complexes and application as fluorescent tracers

ABSTRACT:
The invention relates to macropolycyclic rare earth complexes, namely cryptates which are useful as fluorescent tracers.

US PAT NO: 4,772,548 [IMAGE AVAILABLE] L10: 35 of 38
TITLE: Radioisotopicassay using isotope transfer to **chelator**-target recognition molecule conjugate

ABSTRACT:
A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal **chelating** portion and a **chelating** portion capable of **chelating** with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the **chelating** portion for the radioactive metal ion, wherein prior to contacting the **chelating** portion is unchelated or is **chelated** with a second metal having a binding affinity with the **chelating** portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from the ion transfer material, is disclosed along with various components and kits useful in practicing this method and several variations thereof.

US PAT NO: 4,767,609 [IMAGE AVAILABLE] L10: 36 of 38
TITLE: Therapeutic and diagnostic processes using isotope transfer to **chelator**-target recognition molecule conjugate

ABSTRACT:
A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal **chelating** portion and a **chelating** portion capable of **chelating** with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the **chelating** portion for the radioactive metal ion, wherein prior to contacting the **chelating** portion is unchelated or is **chelated** with a second metal having a binding affinity with the **chelating** portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from the ion transfer material, is disclosed along with various components and kits useful in practicing this method and several variations thereof.

US PAT NO: 4,742,003 [IMAGE AVAILABLE] L10: 37 of 38
TITLE: Human transforming growth factor

ABSTRACT:
Methods and compositions are provided for the recombinant synthesis of the **tumor** growth factor-.alpha. precursor and its fragments. These are useful in therapy and diagnosis, as are antibodies raised by immunization with the **tumor** growth factor-.alpha. precursor and its fragment.

US PAT NO: 4,707,352 [IMAGE AVAILABLE] L10: 38 of 38
TITLE: Method of radioactively labeling diagnostic and therapeutic agents containing a **chelating** group

ABSTRACT:
A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal **chelating** portion and a **chelating** portion capable of **chelating** with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the **chelating** portion for the radioactive metal ion, wherein prior to contacting the **chelating** portion is unchelated or is **chelated** with a second metal having a binding affinity with the **chelating** portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from the ion transfer material, is disclosed along with various components and kits useful in practicing this method and several variations thereof.

=> log y
'-LOG' IS NOT A RECOGNIZED COMMAND

=> log y]
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